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PSYCHOPHARMACOLOGY ABSTRACTS

NATIONAL INSTITUTE OF MENTAL HEALTH

PSYCHOPHARMACOLOGY ABSTRACTS is a publication of the National Clearinghouse for Mental Health Information of the National Institute of Mental Health. It is a specialized information medium designed to assist the Institute in meeting its obligation to foster and support laboratory and clinical research into the nature and causes of mental disorders and methods of treatment and prevention. Specifically, this information service is designed to meet the needs of investigators in the field of psychopharmacology for rapid and comprehensive information about new developments and research results. For information or correspondence with the National Institute of Mental Health concerning Psychopharmacology Abstracts, changes of address, or removal of names from the mailing list see the inside back cover page.

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

51207
AUTHORS: Kozuka, Hiroshi.
ADDRESS: Chemistry Section, National Research Institute of Police Science
TITLE: Identification of narcotics and diagnosis of the addiction. (Unpublished paper).
SOURCEID: National Research Institute of Police Science, 1970. 9 p.

Methods for the identification of narcotics and the diagnosis of addiction are presented. Narcotics form the characteristic microcrystalline precipitates with Marme's, Wagner's, Scheibler's, and Dragendorff's reagents and are used as pretests of narcotics. Heroin is converted back into morphine in the body which is then identified in the urine. Detection of morphine in urine by thin layer chromatography is described. Hydrolysis by hydrochloric acid is followed by chloroform extraction and thin layer or paper chromatography. Rf values are given for morphine, cocaine, heroin, codeine, chlorpromazine, and N-allylnormorphine. The procedure for determining true addiction of a patient as stated by the Narcotic Control Law in 1962 and the suggested diagnostic nalorphine test are described. Blanching, sweating, nausea, vomiting, flow of tears, and gooseflesh are induced in narcotic addicts 20 minutes after nalorphine injection.

55324
AUTHORS: Harrell, William B.
ADDRESS: School of Pharmacy, Texas Southern Univ., Houston, Texas 77004
TITLE: Mannich bases from 1,2-diphenylindolizine: ephedrine and methamphetamine as amine components.
SOURCE: Journal of Pharmaceutical Sciences.
SOURCEID: 59(2):275, 1970.

A report is presented of the synthesis of 2 unique Mannich bases derived from 1,2-diphenylindolizine. Ephedrine and methamphetamine were employed as the secondary amine compounds in the syntheses. Both products showed an initial marked CNS depression. The activity of the methamphetamine derivative was reversed after 1.5 hours to a pronounced CNS stimulation. 5 references. (author abstract modified)

57866 $03
AUTHORS: Marshman, Joan A.; Gibbins, Robert J.
ADDRESS: Addiction Research Foundation, Toronto, Ontario, Canada
TITLE: A note on the composition of illicit drugs.
SOURCE: Ontario Medical Review (Ottawa).
SOURCEID: 37(9):1-3, 1970.

A study of the composition of illicit drugs is presented. One of the most obtrusive features of the use of psychoactive drugs by young people is ignorance of the actual chemical composition of the drugs that are obtained from illicit sources. Samples of illicit drugs were collected and analyzed for their chemical components, employing qualitative methods ascolor tests, thin layer chromatography, infrared spectrophotometry, and gas liquid chromatography. Results showed that there was a marked discrepancy between the alleged composition and the actual composition of the samples. Of the 519 samples for which the alleged composition was availible, 65% were found to contain the drug said to be present. Of the samples alleged to be lysergic acid diethylamide (LSD), 44%contained either LSD with 2 or more contaminants or simply a mixture of products which probably resulted from unsuccessful attempts to synthesize LSD. Mescaline was not found in any of the 58 samples designated by that name. Other results of the study are given. It is apparent that there can be a significant discrepancy between the alleged and real composition of drugs on the illicit market.

58877 $03
AUTHORS: Mesley, R. J.; Evans, W. H.
ADDRESS: Laboratory of the Government Chemist, Cornwall House, Stanford Street, London, S. E. 1, England
TITLE: Infrared identification of some hallucinogenic derivatives of tryptamine and amphetamine.
SOURCE: Journal of Pharmacy and Pharmacology (London).
SOURCEID: 22(5):321-332, 1970.

The use of infrared spectroscopy for the identification of psychotomimetic derivatives of amphetamine and tryptamine is discussed. Numerous characteristic absorptions are assigned on the basis of spectra recorded from 123 bases and salts. These permit the recognition of compounds of these types even when no reference materials or spectra are available. Distinction between the spectra of optically active and racemic forms of some amphetamine derivatives is also possible. 21 references. (author abstract)

58879
AUTHORS: Lippmann, W.
ADDRESS: Department of Biochemical Pharmacology, Ayerst Laboratories, Montreal, Quebec, Canada
TITLE: Blockade of noradrenaline uptake and inhibition of gastric acid secretion by 2-(p-chlorophenyl-2-(pyridyl)hydroxymethyl) imidazoline maleate (Sch-12650).
SOURCE: Journal of Pharmacy and Pharmacology (London).
SOURCEID: 22(5):387-388, 1970.

The compound 2-(p-chlorophenyl-2-(pyridyl)hydroxymethyl) imidazoline maleate (Sch-12650) is as active in antidepressant tests in rats as the currently available antidepressants and possibly acts by interfering with catecholamine uptake mechanisms. The effects of intraperitoneally administered Sch-12650 on the uptake and release of noradrenaline in the heart of the rat are shown. This compound inhibited the basal gastric secretion and at 2.5mg/kg i.p. decreased the gastric acid secretion to half that of controls; Sch-12650 is similar in its action to imipramine. 10 references.

52484
AUTHORS: Schildkraut, Joseph J.
ADDRESS: Massachusetts Mental Health Center, 74 Fenwood Road, Boston, Massachusetts 02115
TITLE: Tranylcypromine: effects on norepinephrine metabolism in rat brain.
SOURCE: American Journal of Psychiatry.
SOURCEID: 126(7):49-55, 1970.

This investigation examines the effects of tranylcypromine on the uptake, release, and metabolism of intracisternally administered tritiated norepinephrine in rat brain. The findings suggest that, in addition to being a potent inhibitor of the enzyme monoamine oxidase, tranylcypromine discharges norepinephrine extraneuronally onto receptors and possibly also inhibits the neuronal reuptake of this amine. These neuropharmacological effects of tranylcypromine may possibly account for the greater clinical efficacy of tranylcypromine in the treatment of some depressed patients and the higher incidence of hypertensive cerebrovascular reactions when this drug is compared with other monoamine oxidase inhibitors. 25 references. (Author abstract)

55322
AUTHORS: Follenfant, M. J.; Robson, R. D.
ADDRESS: Wellcome Research Laboratories, Beckenham, Kent, England
TITLE: The antagonism of adrenergic neurone blockade by amphetamine and dexamphetamine in the rat and guinea-pig.
SOURCE: British Journal of Pharmacology (London).
SOURCEID: 38(4):792-801, 1970.

The antagonism of adrenergic neuron blockade by amphetamine and dexamphetamine was studied in the rat and guinea pig. Sympathetically induced vasoconstriction of the in vitro perfused mesenteric vessels and contracture of the inferior eyelid of rats were used to examine the adrenergic neuron blockade and the ability of amphetamine or dexamphetamine to restore sympathetic function at both short and long times after administration of several antihypertensive agents (bretylium, bethanidine, guanethidine, reserpine, and phenoxypropylguanidine. The last of these lowers blood pressure in hypertensive rats and dogs, apparently without causing direct impairment of sympathetic nerve transmission. The response of hypogastric nerve stimulation of the vas deferens preparation of guinea pigs which had received prior doses of guanethidine or bretylium was also used to study adrenergic neuron blockade and the influence of amphetamine. 18 references. (author abstract modified)

55394
AUTHORS: Marmo, E.; Di Mezza, F.; Imperatore, A.; Di Giacomo, S.
ADDRESS: Institut fur Pharmakologie und Toxikologie der Universitat, Via Cinarosa 37, 80 127 Naples, Italy
TRTITLE: /Metoclopramide and the musculature of esophagus, stomach, intestine, spleen, trachea, gall and urinary bladders: in vitro studies./
TITLE: Metoclopramid und die Muskulatur von Osophagus, Magen, Darm, Milz, Trachea, Gallen- und Harnblase: Untersuchungen in vitro.
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 29(1):18-27, 1970.

Human organs and those of frogs, guinea pigs, rats, cats, rabbits and dogs were used in the reported in vitro studies on the effect of N-(diethylaminoethyl)-2-methoxy-4-amino-5-chlorobenzamide on muscle. In low concentrations, the substance has a stimulating effect on smooth muscle, and in high concentrations it has a depressant effect. There is a papaverinelike general antagonizing effect in high concentrations, with respect to acetylcholine,

histamine, 5-hydroxytryptamine and norepinephrine. 42 references. (author abstract modified)

55396
AUTHORS: Holtermann, W.; Lochner, W.
ADDRESS: Physiologisches Institut der Universitat, 4 Dusseldorf, Ulenbergstrasse 123, Germany
TRTITLE: /On the analysis of cardiac beta-receptors: studies on the base of dose-effect curves for isoprenaline, propranolol, and KL 255./
TITLE: Zur Analyse der beta-Receptoren des Herzens: Untersuchungen an Hand der Dosis-Wirkungs-Kurven von Isoprenalin, Propranolol und KL 255.
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 20(1):8-12, 1970.

Results of experiments on 138 isolated guinea pig hearts indicate that there is a single type of beta-receptor in the heart. Concentration effect curves were established for N-isopropylnorepinephrine sulfate with respect to changes of systolic peak pressure in the left ventricle, differential ratio dp/dt max, oxygen consumption, coronary blood flow and rate of the heart beat: the same kinds of values were obtained for all parameters. Qualitatively and quantitatively, the competitive antagonism of 1-(isopropylamino)-3-(1-naphthyloxy)-2-propanol and 1-(2'-chloro-3'-methylphenoxy)-3-tert.-butylamino-propan-2-ol hydrochloride with respect to isoprenaline was also of the same kind, again supporting the hypothesis of a single type of beta-receptor in the heart. 20 references. (author abstract modified)

55397
AUTHORS: Lenke, D.; Brock, N.
ADDRESS: Pharmakologische Abteilung der Asta-Werke AG, 4812 Brackwerde i. Westf., Germany
TRTITLE: /On the pharmacology of ispropylidene-proscillaridin./
TITLE: Zur Pharmakologie von Isopropyliden-Proscillaridin.
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 20(1):1-7, 1970.

Comparative pharmacological studies of isopropylidene -proscillaridin and proscillaridin are presented. The positive inotropic action of both glycosides was tested in vitro on the electrically stimulated papillary muscle of the guinea pig. The action on the contractility of the left ventricle was tested on guinea pigs and cats in vivo. The glycosides have almost the same effect on the guinea pig in vitro and in vivo. Cardiotoxicity was demonstrated in cats and guinea pigs by intravenous or intraduodenal infusion: the minimal toxic dose of isopropylidene -proscillaridin when given intravenously was 74% higher than that of proscillaridin alone. Enteral activity of isopropylidene - proscillaridin was also 3.75 times higher than that of proscillaridin. Proscillaridin alone or in combination with isopropylidene inhibited active transport of sodium and potassium ions through the human erythrocyte membranes. Isopropylidene - proscillaridin was highly toxic to rats. 21 references. (author abstract modified)

55519
AUTHORS: Massarani, E.; Nardi, D.; Magistretti, M. J.
ADDRESS: Research Division, Recordati s. a. s., Via Civitali 1, Milan, Italy
TITLE: 4-(Beta-benzoylvinyl)-antipyrine derivatives with antiphlogistic and analgesic activity.
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 19(12):2020-2022, 1969.

A series of 4-(beta-benzoylvinyl)-antipyrine derivatives were prepared and tested pharmacologically on rats and rabbits with respect to toxicity, smooth muscle relaxing activity, antitussive

effect, analgesic action, antipyretic effect, and antiinflammatory effect. Some of these substances showed antiinflammatory and analgesic activity comparable to those of aminopyrine and phenylbutazone, with lower toxicity. Substitution with methyl in the 2 position and of vinyl in the 4 position was found to be important. 7 references. (author abstract modified)

55579
AUTHORS: Mazurkiewicz-Kwilecki, I. M.; Bonagnoli, A.
ADDRESS: Dept. of Pharmacology, Faculty of Medicine, Univ. of Ottawa, Ottawa, Canada
TITLE: Cardiac catecholamine levels and blood pressure after chronic treatment with beta-adrenergic blocking agents.
SOURCE: Journal of Pharmacy and Pharmacology (London).
SOURCEID: 22(3):235-237, 1970.

Experiments were performed to establish whether chronic treatment with beta-adrenergic blocking agents would cause changes in endogenous catecholamine levels in the heart, brain, and spleen of normotensive, nonanesthetized rats, and whether there would be any correlation between these changes and the systolic blood pressure. The effect of such agents on brain and spleen was not consistent in the present study, and it would be difficult to speculate on its significance. No correlation was found between the changes in endogenous catecholamine level in the heart and blood pressure of experimental animals. In spite of the significantly lower endogenous catecholamine level in the heart, the systolic blood pressure of rats treated with beta-adrenergic blocking agents did not significantly differ from control animals. 12 references.

55580
AUTHORS: Mercier, J.; Dessaigne, S.; Manez, J.
ADDRESS: Laboratoire de Pharmacologie, Faculte de Medecine et de Pharmacie, Boulevard d'Ales, F 13 Marseille Ve, France
TITLE: Neurophysiological study of dipotassium chlorazepate (4306 CB).
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 20(1):125-127, 1970.

Dipotassium chloroazepate (4306 CB, Tranxilium) synchronizes neocortical electric activity. This synchronization is due to a depressive action on reticular excitability which is reflected in a decreased duration of cortical activation reactions provoked by harmful stimulation. The 4306 CB slightly decreases cortical excitability. Its antipentetrazoleactivity is good, a fact which indicates that this product is probably active in the treatment of petit mal. The considerable decrease in hypertensive reaction following a painful stimulus confirms synaptic blocking at the reticular level. The depressive actions exerted by 4306 CB on hippocampal and posterior hypothalamic excitability, together with that already evidenced on the reticular activating system, possibly explain the mechanism of the antianxiety effect exerted by this substance. 8 references. (author abstract modified)

55581
AUTHORS: Brunaud, M.; Navarro, J.; Salle, J.; Siou, G.
ADDRESS: Centre de Recherces CLIN-BYLA, 20, rue des Fosses St. Jacques, Paris Ve, France
TITLE: Pharmacological, toxicological, and teratological studies on dipotassium-7-chloro-3-carboxy-1,3-dihydro-2,2-dihydroxy-5-phenyl-2H-1,4-benzodiazepine-chlorazepate (dipotassium chlorazepate, 4306 CB), a new tranquillizer.
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 20(1):123-125, 1970.

Dipotassium chlorazepate (4306 CB) exerts a muscle relaxing and ataractic action. It possesses a distinct anticonvulsive potency and

modified only slightly the motility, spontaneous or provoked, by psychomotor stimulants. It protects mice and cats against the morphine crisis and the convulsions provoked by strychnine. It potentiates the hypnotic action of phenobarbital and, at average doses, improves conditioned reflexes. It does not significantly modify respiratory movements. At large doses it exerts an analgesic effect and increases sodium excretion. Its acute toxicity in the mouse and rat is very low. Studies on chronic toxicity in the rat, rabbit, and dog showed no histological lesions attributable to the product and only a slight decrease in the red cell count of the rat treated at high doses. No teratogenic effect was observed in the 3 species. 5 references. (author abstract modified)

55582
AUTHORS: Sabelli, Hector C.; Priest, W. Curtis.
ADDRESS: Dept. of Pharmacology, Chicago Medical School, 2020 West Ogden Ave., Chicago, Ill. 60612
TITLE: Water structure in anesthetic action: time-dependence D20 effects on nerve.
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 20(1):80-88, 1970.

The influence of D20 replacements of H20 in frog Ringer's solution on the axonal effects of ether and ethanol were studied as an in vitro model for analysis of the role of water in narcosis. D20 (75% to 99%) replacements markedly prolonged survival of frog sciatic nerve; on long exposure (8 days) threshold was somewhat reduced, spike amplitude was relatively increased, and hyperexcitability during rapid stimulation or following supramaximal stimulation was relatively augmented. Short exposures (10 to 30 minutes) only depressed frequency hyperexcitability. The results suggested early direct solvent effects attributable to the greater ice likeness of D20 relative to H20, followed by slower changes resulting from deuteration of tissue constituents. Conduction block by ether or ethanol was antagonized by concurrent application of D20 (but not by prior 24 hour exposure to D20), suggesting that increased structural order in water antagonized narcosis. Concurrent application of D20 also antagonized conduction block by nicotine and ouabain, but had little effect on block by cocaine, procaine, and lidocaine. Conduction blocking time by cocaine was markedly reduced by prior 24 hour exposure to D20 Ringer's. 32 references. (author abstract modified)

55583
AUTHORS: Sabelli, H. C.; Giardina, W. J.
ADDRESS: Dept. of Pharmacology, Chicago Medical School, 2020 West Ogden Ave., Chicago, Ill. 60612
TITLE: Tryptaldehydes (indoleacetaldehydes) in serotonergic sleep of newly hatched chicks.
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 20(1):74-80, 1970.

Tryptaldehyde (indoleacetaldehyde), 5-hydroxytryptaldehyde, tryptophol, and 5-hydroxytryptophol (metabolites of tryptamine and serotonin catalyzed by monoamine oxidase were as effective as the amines in inducing sleep in newly hatched chicks. The monoamine oxidase inhibitor (MAOI) pargyline induced drowsiness and reduced (but did not block) the sleep promoting effect of 5-hydroxytryptophan, tryptamine, tryptophol and, to a lesser extent, that of serotonin and tryptaldehyde. Nicotine induced typical sleeplike behavior followed by hyperactivity; both effects were reduced by pargyline pretreatment. These results suggest that tryptaldehydes are biologically active and may be partly responsible for the behavioral effects of their amine precursors. It is speculated that the behavioral effects of an MAOI may be partly due to inhibition of the synthesis of deaminated derivatives of biogenic amines, and that tryptaldehydes may be the deaminated products of tryptamines postulated by Jouvet to trigger REM sleep. 32 references. (author abstract modified)

55584
AUTHORS: Sabelli, H. C.; Giardina, W. J.; Alivisatos, S. G. A.
ADDRESS: Dept. of Pharmacology, Chicago Medical School, 2020 W. Ogden Ave., Chicago, Ill. 60612
TITLE: Influence of serotonin and related substances upon photic-evoked potentials of rabbit: evidence for biological activity of the aldehyde derivative.
SOURCE: Arzneimittel-Forschung (Wurttemburg).
SOURCEID: 20(1):68-74, 1970.

The intraventricular administration of serotonin (5HT) or its derivative 5-hydroxyindole-3-acetaldehyde (5HTA) and the systemic injection of its precursor 5-hydroxytryptophan (5HTP) initially enhanced and later depressed the slow negative component of the photic evoked response in unanesthetized rabbits. This biphasic effect was characteristic for serotonergic drugs and not shared by adrenergic and cholinergic agents. Monoamine oxidase inhibitors (MAOI) prevented the initial enhancing effects of 5HTP but augmented its late depressant effect. MAOI partially blocked the evoked potential changes induced by 5HT and by 5HTA. The finding that 5HTA induced serotoninlike effects in the same dose range and as promptly as 5HT, linked to the additional evidence that MAOI block certain effects of 5HT, 5HTA, and 5HTP, suggest the need for further explanation of the possible biological role of the deaminated derivatives of serotonin. 27 references. (author abstract modified)

55585
AUTHORS: Kobayashi, Shinsaku; Hasegawa, Kazuo; Mori, Masahiro; Takagi, Hiromu.
ADDRESS: Central Research Laboratories, Sankyo Co., Ltd., Shinagawa-ku Tokyo, Japan
TITLE: Pharmacological studies on a new specifically potent antitussive agent, 14-hydroxydihydro-6-beta-thebainol-4-methylether (oxymethebanol).
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 20(1):43-46, 1970.

14-Hydroxydihydro-6-beta-thebainol-4-methylether (oxymethebanol) has shown specifically potent antitussive activities in experimentally induced coughing. The antitussive potency of this compound was 14 to 25 times greater than that of codeine phosphate in mechanical stimulation in guinea pigs, 5 to 10 times greater using the ammonia gas method in guinea pigs, and 50 times greater in mechanical stimulation in dogs. The analgesic potency of this compound was twice as potent as that of codeine phosphate in guinea pigs. Adverse side-effects such as respiratory depression, hypotension, constipation, and physical dependence liability were induced less by oxymethebanol than by codeine. Such advantages of oxymethebanol suggest its wide usefulness as a potent antitussive agent. 13 references. (author abstract modified)

55586
AUTHORS: Kase, Y.; Wakita, Y.; Yuizono, T.; Kito, G.; Kikuchi, K.
ADDRESS: Dept. of Chemico-Pharmacology, Faculty of Pharmaceutical Sciences, Kumamoto Univ., Kumamoto, Japan
TITLE: On the sites of antitussive action of N-(2-picolyl)-N-phenyl-N-(2-piperidinoethyl)amine (TAT-3).
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 20(1):37-43, 1970.

The sites of antitussive action of N-(2-picolyl)-N-phenyl-N-(2-piperidinoethyl)amine hydrochloride (TAT-3) were investigated. The antitussive action of TAT-3 is due to selective depression of the cough center per se. In addition to this, a reliable spasmolytic action on the bronchial muscles may contribute to the antitussive activity. When TAT-3 was given by the

routes leading to the brain stem, far smaller doses were sufficient to obtain the same effect as that by intravenous administration. It exerted no effect on the sensory receptors for cough reflex in the tracheal mucosa and on pulmonary stretch receptors. The antitussive effect of the drug was not influenced by decerebration. It depressed the centrally induced coughs in antitussive effective doses which were able to depress peripherally induced coughs; it had no pronounced effect on the respiratory center with the same dose. It showed no effect on the descending respiratory pathways extending from the cervical cord to the respiratory muscles. It possesses a significant spasmolytic action on histamine induced contraction of bronchial muscles in antitussive effective doses. 32 references. (author abstract modified)

55587
AUTHORS: Henning, M.; Rubenson, A.
ADDRESS: Dept. of Pharmacology, Univ. of Goteborg, S-40033, Goteborg, Sweden
TITLE: Evidence for a centrally mediated hypotensive effect of L-dopa in the rat.
SOURCE: Journal of Pharmacy and Pharmacology (London).
SOURCEID: 22(3):241-243, 1970.

Evidence for a centrally mediated hypotensive effect of L-dopa in the rat is presented. Systemic administration of L-dopa to rats results in a pronounced increase in mean arterial blood pressure which seems to be due to peripheral actions. The centrally mediated hypotensive action is unmasked following inhibition of the peripheral metabolism of L-dopa to catecholamines. The results make it less probable that this central effect is mediated via dopamine, but indicate the importance of noradrenergic mechanisms. Actions of this kind may be involved in episodes of postural hypotension or permanent lowering of blood pressure sometimes observed during oral treatment of parkinsonian patients with L-dopa. 17 references.

55739
AUTHORS: Strubelt, O.; Vogelberg, W.; Zetler, G.
ADDRESS: Institut fur Pharmakologie der Medizinischen Akademie, 24 Lubeck, Ratzeburger Allee 160, Germany
TRTITLE: /Inhibition of the stimulating effect of methamphetamine and morphine on mouse by influencing the endogenous catecholamines./
TITLE: Hemmung der stimulierenden Wirkung von Methamphetamin und Morphin auf die Maus durch Beeinflussung endogener Katecholamine.
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 20(1):32-37, 1970.

Experiments with mice are reported which indicate that the central nervous system stimulation of morphine and methamphetamine is the effect of an indirect mechanism operating through the central catecholamines. Reserpine abolished the stimulating effect of 30mg/kg morphine, but not that of 4mg/kg methamphetamine. Tetrabenazine antagonized both substances; it depletes the central catecholamines. Alpha-methyl-p-tyrosine completely suppressed the effects of morphine and methamphetamine; this substance blocks biosynthesis of norepinephrine. In doses that did not block the biosynthesis of norepinephrine but that depleted brain catecholamines, it did not affect the action of morphine and methamphetamine. 56 references. (author abstract modified)

55740
AUTHORS: Sandor, Peter; Kovach, Arisztid G. B.; Horvath, K. B.; Szentpetery, G. B.; Clauder, Otto.
ADDRESS: Institut fur Angewandte Botanik und Histogenetik der Eotovos Lorand Universitat, Budapest, Hungary
TRTITLE: /Pharmacological studies on the action of synthetic alpha-methyl-pyrryl-ketone on the CNS and on circulation./

TITLE: Pharmakologische Untersuchungen uber die Wirkung von Synthetischem alpha-Methyl-pyrryl-keton auf das Zentralnervensystem und den Kreislauf.
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 20(1):29-32, 1970.

Comparative studies using rats, cats and dogs concerning the effects of synthetic alpha-methyl-pyrryl-ketone showed that arterial pressure is reduced as a consequence of decreased responsiveness of the sympathetic centers and of vasodilatation of vessels in the abdomen. The drug has low toxicity and it is strongly sedative in its effect. It does not inhibit conditioned reflexes. It potentiates the effects of barbiturates. When given to rats in the same dosage as hexobarbital it tripled the average sleeping time. 12 references. (author abstract modified)

55756
AUTHORS: Vedernikov, Yu. P.
ADDRESS: Laboratory of Subcellular Ecology, Institute of Plant and Animal Ecology, Ural's Branch of USSR Academy of Sciences, Sverdlovsk, USSR
TITLE: The role of brain catecholamines in morphine analgesic action in morphine tolerant rats.
SOURCE: Journal of Pharmacy and Pharmacology (London).
SOURCEID: 22(3):238-239, 1970.

Experiments on morphine tolerant rats to support the role of norepinephrine in morphine analgesia are described. The experimental white female rats, weighing 180 to 230 gm, were made tolerant to a test dose of morphine (5mg/kg) after 20 days of successive subcutaneous injections of 10mg/kg of morphine. The analgesic activity was assessed using the change in pain threshold to mechanical pressure of the tail. By this test, before tolerance to the test dose was developed, the pain threshold after morphine was 100 mm Hg (top limit); after tolerance, the pain threshold showed no appreciable change from base value. Cocaine hydrochloride, pyrogallol or tryptophan increased the analgesic action on the pain threshold. Iproniazid increased the effect of the morphine test dose slightly more. The most pronounced action on the restoration of the ability of morphine to elevate the pain threshold was shown by amphetamine. It seems that the inhibition of any mechanism by which norepinephrine is normally inactivated is accompanied by the reappearance of analgesia to the test dose of morphine in tolerant rats. The marked potentiation by amphetamine of the analgesia induced by the morphine test dose can be explained by its action in releasing brain catecholamines; the decrease of this action after the development of tolerance is to be attributed to the loss of ability by morphine to release norepinephrine completely. 3 references.

56238
AUTHORS: Cochin, Joseph.
ADDRESS: Dept. of Pharmacology, Boston Univ. School of Medicine, Boston, Mass.
TITLE: Possible mechanisms in development of tolerance.
SOURCE: Federation Proceedings.
SOURCEID: 29(1):19-27, 1970.

Possible mechanisms in the development of tolerance to the effects of narcotic analgesics are discussed. Various hypotheses previously proposed to explain such tolerance are reviewed. Experimental evidence to support these hypotheses is both meager and inconclusive. Laboratory experiments with mice were conducted which indicate that tolerance is a threshold phenomenon that can be initiated by a single injection and which takes time to incubate. The effects may persist for very long periods and even be transferred to succeeding generations. Certain compounds (e.g., cycloheximide) which are known to repress protein synthesis and immune reactions also interfere with the development of tolerance and dependence. The sympathetic nervous system and, especially, certain catecholamines

may be implicated in some aspects of tolerance. The highly inconclusive nature of experiments concerning tolerance is emphasized. 55 references.

56610
AUTHORS: Segawa, Tomio.
ADDRESS: Depart. of Pharmacology, Kyoto University, Sakyo-ku, Kyoto, Japan
TITLE: Effects of reserpine and desipramine on the uptake and subcellular distribution of 5-hydroxytryptamine in rabbit brain stem after intravenous administration of 5-hydroxytryptophan.
SOURCE: Japanese Journal of Pharmacology (Kyoto).
SOURCEID: 20(1):87-91, 1970.

Subcellular distribution of 5-hydroxytryptamine (5-HT) in rabbit brain stem after intravenous administration of 5-hydroxytryptophan (5-HTP) (50mg/kg) was studied. The 5-HTP induced increase of 5-HT was more prominent in the microsomal (P3) and axonal (S3) fractions. Pretreatment with reserpine (3mg/kg, i.p., 15 hours before death) inhibited the increase, particularly in the synaptic vesicular (P2V) fraction. Pretreatment with the monoamine oxidase inhibitor pheniprazine (3mg/kg, i.p., 1 hour before death) restored 5-HT after 5-HTP administration even in reserpinized rabbits. Desipramine (20mg/kg, i.p., 50 minutes before death) could further increase the amount of 5-HTP induced 5-HT, although it inhibited the increase in the P2V fraction. 9 references. (author abstract modified)

57033
AUTHORS: Remmer, H.; Schuppel, Rainer.
ADDRESS: Institute of Toxicology, Tubingen University, Tubingen, West Germany
TITLE: The influence of ethanol on drug metabolism.
SOURCE: In: Popham, R., Alcohol and alcoholism.
SOURCEID: Toronto, University of Toronto Press, 1970. 421 p. (p. 80-85).

The duration of anesthesia is considerable shortened if rats are pretreated with ethanol for 8 to 14 days. There is also a marked difference in sleeping time after the intraperitoneal administration of hexobarbital to rats pretreated with ethanol. The best evidence for tolerance by an increased metabolism of barbiturates after pretreatment with ethanol is the fact that liver supernatant metabolizes hexobarbital in vitro a little faster if it is prepared from the livers of rats treated with ethanol. An alcoholic intake for several weeks may produce an accelerated metabolism of drugs. The opposite may occur if a higher alcohol level prevails in the organism. Ethanol added in vitro to liver supernatant causes an inhibition of the oxidative demethylation of monomethylaminoantipyrine. A concentration of ethanol which can be easily achieved in man after intake of alcohol leads to an inhibition of the oxidation rate. 4 references.

58192
AUTHORS: Haber, B.; Sze, P. Y.; Kuriyama, K.; Roberts, E.
ADDRESS: Div. of Neurosciences, City of Hope Medical Center, Duarte, Calif. 91010
TITLE: GABA as a repressor of L-glutamic acid decarboxylase (GAD) in developing chick embryo optic lobes.
SOURCE: Brain Research (Amsterdam).
SOURCEID: 18(3):545-547, 1970.

Gamma-aminobutyric acid (GABA) and aminooxyacetic acid hemihydrochloride (AOAA) were injected into chick embryos to determine whether elevated cerebral GABA levels repress L-glutamic acid decarboxylase (GAD I). A marked decrease in GAD I activity was observed in the optic lobes 24 hrs after the injection of GABA, the earliest postinjection period studied. Progressively smaller

decrements in GAD I activity were observed at 48 and 72 hrs. Injection of 200 micrograms AOAA had a smaller repressive effect on GAD I activity of optic lobes than 100mg of GABA. Gamma-aminobutyric acid content increased dramatically in the optic lobes following a single injection of GABA, and a maximal increase in GABA levels coincided with a maximal decrement in GAD I. Similar results were obtained using AOAA. Measurement of GAD II activity in optic lobes at similar time intervals following a single injection of GABA or AOAA showed that this form of GAD is also repressed by both agents, maximal repression being observed at 24 hrs, at which time GABA content was maximally elevated. Repression of GAD by GABA may be a specific effect and not a reflection of a general inhibition of protein synthesis. 13 references.

58383
AUTHORS: Sofia, R. Duane; Salama, Andre I.
ADDRESS: University of Pittsburgh, School of Pharmacy, Dept. of Pharmacology, 1015 Salk Hall, Pittsburgh, Pa. 15213
TITLE: Circadian rhythm for experimentally-induced aggressive behavior in mice.
SOURCE: Life Sciences (Oxford).
SOURCEID: 9(6):331-338, 1970.

Male Swiss albino mice were used to determine whether experimentally induced aggressive or fighting behavior would exhibit a circadian rhythm similar to and in fact, superimposable on the circadian rhythm found for locomotor activity. Alterations in brain levels of norepinephrine and/or 5-hydroxytryptamine in fighting mice when compared with non-fighting controls throughout a 24 hour period were studied. Mice consistently displayed similar 24 hour rhythms for both electric footshock - induced fighting behavior and locomotor activity when housed under 12 hours of light and 12 hours of darkness. These rhythms might possibly by controlled via exogenous factors since continuous light for 24 hours prior to testing almost obliterated them. Norepinephrine and serotonin levels were virtually unaffected in mice exposed to either lighting schedule. 6 references. (author abstract modified)

58571
AUTHORS: Huang, C. L.; Yeh, J. A.; Hsu, S. Y.
ADDRESS: Department of Pharmacology, School of Pharmacy, University of Mississippi, University, Mississippi 38677
TITLE: Distribution, excretion, and metabolism of 14C-labeled quaternary ammonium salt of mepazine and promethazine in rats.
SOURCE: Journal of Pharmaceutical Sciences.
SOURCEID: 59(6):772-775, 1970.

Studies on the biological fate and antimicrobial activity of mepazine and promethazine methiodide are presented. Synthesis of 14C-methiodide and estimation of the unchanged compound in biological materials are described. After intraperitoneal administration, the majority of these compounds was excreted in feces. The radioactivity in the liver and kidneys prevailed over other organs. Blood levels were low but above the significant level in both compounds. Brain level of promethazine methiodide-14C was detectable but that of mepazine methiodide-14C was insignificant. These compounds displayed a significant antimicrobial activity. 15 references. (author abstract)

58604
AUTHORS: Vikhlyayev, Yu. I.; Klygul', T. A.; Astakhova, A. V.
ADDRESS: Laboratoriya Psikhofarmakologii Instituta Farmakologii i Khimioterapii AMN SSSR, Moscow, U.S.S.R.
TRTITLE: /Anticonvulsive properties of some benzodiazepine derivatives./
TITLE: O protivosudorozhnykh svoystvakh nekotorykh proizvodnykh benzodiazepina.

SOURCE: Farmakologiya i Toksikologiya (Moskva).
SOURCEID: 33(2):149-154, 1970.

Effects of nitrazepam and chlordiazepoxide on strychnine were compared to those of diphenylhydantoin, benzonal, phenobarbital and trimethadione on electrically induced convulsions in mice. Antiepileptic activity of benzodiazepine compounds was found to closely resemble that of trimethadione, but with an intensive anti - metrazol activity differing significantly from diphenylhydrazide or benzonal. In contrast to phenobarbital, benzodiazepine compounds exerted a high degree of activity against convulsions induced by electrical stimulation of the spinal cord. Phenobarbital produced a more specific effect on convulsions induced by stimulation of brain. 13 references. (author abstract modified)

58605
AUTHORS: Ostrovskaya, R. U.; Artemenko, G. N.; Rayevskiy, K. S.
ADDRESS: Laboratoriya Farmakologii Nervnoy Sistemy Instituta Farmakologii AMN SSSR, Moscow, U.S.S.R.
TRTITLE: /Neurotropic properties of aminohydroxyacetate and gamma-aminohydroxybutyric acid./
TITLE: O neyrotropnykh svoystvakh aminooksiuksusnoy i gamma-aminooksimaslya-noy kislot.
SOURCE: Pharmakologiya i Toksikologiya (Moskva).
SOURCEID: 33(2):137-142, 1970.

The neurotropic effects of aminohydroxyacetate (AHA) and gamma-aminohydroxybutyric acid (GAHBA) were assessed. In both mice and rabbits, both substances potentiate the effects of sodium thiopental, barbital and sodium hydroxybutyrate. The mechanism of potentiation of the narcotic effect comprises both direct and indirect components. AHA and GAHBA possess a synchronization effect and potentiate GABA, as measured by the electroencephalogram. Both AHA and GAHBA have protective effects against convulsions induced by semicarbazide and exert protective action in conditions and procedures which reduce the content of GABA in the brain. It is suggested that in the mechanism of action of AHA and GAHBA, an important role is played by the increase in GABA content in brain structures. 12 references. (author abstract modified)

58798
AUTHORS: Schubert, Johan; Nyback, Henrik; Sedwall, Goran.
ADDRESS: Department of Psychiatry, St. Goran's Hospital, S-104 01 Stockholm 60, Sweden
TITLE: Effect of antidepressant drugs on accumulation and disappearance of monoamines formed in vivo from labelled precursors in mouse brain.
SOURCE: Journal of Pharmacy and Pharmacology (London).
SOURCEID: 22(2):136-139, 1970.

The effect of tritiated tryptophan on C-14-labeled tyrosine (i.v.) was measured in relation to the accumulation and disappearance of tritiated 5-hydroxytryptamine, dopamine and noradrenaline formed in mouse brain. The results demonstrated significant effects of dimethylated antidepressants on brain 5-hydroxytryptamine metabolism but not on noradrenaline or dopamine metabolism. Incontrast, the monomethylated derivatives had a significant effect on the metabolism of brain noradrenaline but not on that of dopamine or 5-hydroxytryptamine. The reduced amine accumulation and disappearance indicate that dimethylated and monomethylatedantidepressants decelerate synthesis and turnover of the transmitter in serotoninergic and noradrenergic neurons, respectively. Such an effect could be mediated by the inhibition of amine reuptake, if this leads to an increased receptor stimulation which by a negative feedback mechanism inhibits nerve impulse activity in the presynaptic neuron. 13 references.

58799
AUTHORS: Meek, James; Werdinius, Bengt.
ADDRESS: Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg 33, Sweden
TITLE: Hydroxytryptamine turnover decreased by the antidepressant drug chlorimipramine.
SOURCE: Journal of Pharmacy and Pharmacology (London).
SOURCEID: 22(2):141-143, 1970.

The accumulation of 5-hydroxyindoleacetic acid (5-HIAA) in rat brain after probenecid (200 mg/kg, i.p.) blockade of 5-HIAA efflux in rats pretreated with chlorimipramine (15 mg/kg i.p.) and untreated controls was determined. The 5-hydroxytryptamine (5-HT) turnover rate of rats treated with chlorimipramine was only 30% of that of control animals. These findings lead further support to the possibility that antidepressant drugs may act, at least partly, by altering some effect of 5-HT in brain. 13 references.

58800
AUTHORS: Estler, C.-J.; Ammon, H. P. T.
ADDRESS: Pharmakologisches Institut der Universitat Erlangen-Nurnberg, Universitatsstrasse 22, D-8520 Erlangen, Germany
TITLE: Antagonistic effects of dopa and propranolol on brain glycogen.
SOURCE: Journal of Pharmacy and Pharmacology (London).
SOURCEID: 22(2):146-147, 1970.

Female mice were treated with (plus or minus)-propranolol (5 micrograms/g, i.p.) or with (plus or minus)-dopa (300 micrograms/g, i.v.) or with both. Propranolol did not significantly affect the spontaneous motor activity of single mice, but the glycogen content of the brain was increased. Dopa, at this dosage, much reduced the motor activity of mice and temporarily lowered the glycogen content of the brain. Where given simultaneously with propanolol, dopa prevented the increase of the glycogen content within the first 30 minutes after its injection. Later, the glycogen rose at the same rate as in animals treated with propranolol alone. Glycogen metabolism of the brain must be controlled by adrenergic mechanisms, and the increase of brain glycogen produced by propranolol is the result of the beta receptor blocking rather than the central depressant properties of propranolol. Thus, the effects of dopa are in contrast to those of other central depressants, which raise the glycogen content of the brain, but resemble those of ethanol. 12 references.

58879
AUTHORS: Horita, A.; Hamilton, A. E.
ADDRESS: Department of Pharmacology, School of Medicine, University of Washington, Seattle, Washington 98105
TITLE: Potentiation of the central actions of 5-hydroxytryptophan in rabbits by DL-alpha-hydrazino-alpha-methyldopa.
SOURCE: Journal of Pharmacy and Pharmacology (London).
SOURCEID: 22(5):389-391, 1970.

DL-Alpha-hydrazino-alpha-methyldopa (HMD) is effective in potentiating both the central effects of dopa in animals and some of the antiparkinson actions in man. The mechanism of this potentiation is based on the ability of HMD to inhibit peripheral L-aromatic aminoacid decarboxylase, but presumably not of that in the central nervous system, thus permitting more of the dopa to reach the brain, where decarboxylation to dopamine occurs. The behavioral and hyperthermic actions of 5-hydroxytryptophan in the rabbit were used as end points in the described experiments. Results point to a possible use for drugs such as HMD as an adjunct to 5-hydroxytryptophan therapy in Down's syndrome. 10 references.

58942
AUTHORS: Stark, Paul; Fuller, Ray W.; Hartley, Lawrence W.;

Schaffer, Robert J.; Turk, John A.
ADDRESS: Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, Indiana 46206
TITLE: Dissociation of the effects of p-chlorophenylalanine on self- stimulation and on brain serotonin.
SOURCE: Life Sciences (Oxford).
SOURCEID: 9(1):41-48, 1970.

Para-chlorophenylalanine inhibited self-stimulation in rats and dogs with chronically implanted electrodes in the posterior hypothalamus. Para-chlorophenylalanine lowered serotonin in bothspecies, but had little or no effect on brain norepinephrine. The depression of self-stimulation and the lowering of brain serotonin levels were not related temporally. Self-stimulation in rats was depressed at 1 and 6 hrs, but had returned to normal by 24 hrs; in contrast, brain serotonin was only slightly lowered by 6 hrs and markedly lowered by 24 hrs. In dogs, self-stimulation was depressed at 6 and 24 hrs but had returned almost to normal at 96 hrs; brain serotonin, on the other hand, declined steadily throughout the 96 hr period. The depression of self-stimulation by para-chlorophenylalanine is not a consequence of its depletion of brain serotonin. 12 references. (author abstract modified)

56237
AUTHORS: Thompson, T.; Pickens, R.
ADDRESS: Univ. of Minnesota, Minneapolis, Minn.
TITLE: Stimulant self-administration by animals: some comparisons with opiate self-administration.
SOURCE: Federation Proceedings.
SOURCEID: 29(1):6-12, 1970.

Stimulant self-administration by laboratory animals, particularly rats, is compared with opiate self-administration. Stimulant self-administration is affected by the type of drug, dosage per infusion, the schedule of drug reinforcement, and the presence of other drugs. The duration and volume of infusion appear to be relatively insignificant variables. Stimulant self-administration differs from opiate self-administration in several respects. Acquisition of stimulant self-administration is very rapid, the pattern of stimulant infusions is extremely stable and invariable, there is a tendency for stimulant self-administration to be cyclic, and during extinction of stimulant self-administration there is very little persistence of response, but a tendency to respond at a very high rate for a short time. Opiate self-administration is characterized by the opposite indications in all cases. These differences may be related to the distinctions between drugs producing physical dependence and those that do not. 28 references. (author abstract modified)

56240
AUTHORS: Schuster, C. R., Jr.
ADDRESS: Dept. of Pharmacology, Univ. of Michigan, Ann Arbor, Mich.
TITLE: Psychological approaches to opiate dependence and self-administration by laboratory animals.
SOURCE: Federation Proceedings.
SOURCEID: 29(1):2-5, 1970.

Psychological approaches to opiate dependence and self-administration by laboratory animals are discussed. Experiments were conducted to determine whether physical dependence upon opiates was a necessary antecedent condition for animals to self-administer the drug, as an aid in assessing the contributions of conditioning to the problem of relapse in human narcotic addicts. The subjects were 5 adult rhesus monkeys surgically prepared with chronic indwelling jugular catheters. They were conditioned to work for food, water, and drug reinforcement, responding to lights at prescribed times of the day. It was concluded that morphine can act as a positive reinforcer, independently of its ability to relieve the withdrawal syndrome, and that the reinforcing efficacy of morphine is markedly amplified when animals are undergoing withdrawal. 13 references.

56934
AUTHORS: Ferguson, James; Henriksen, Steven; Cohen, Harry; Mitchell, George; Barchas, Jack; Dement, William.
ADDRESS: Dept. of Psychiatry, Stanford University School of Medicine, Stanford, California 94305
TITLE: "Hypersexuality" and behavioral changes in cats caused by administration of p-chlorophenylalanine.
SOURCE: Science.
SOURCEID: 168(3930):499-501, 1970.

Observations of the behavior of 26 male cats before, during and after daily administration of the tryptophan hydroxylase inhibitor, para-chlorophenylalanine, revealed that hypersexuality, increased aggression and perceptual disorientation are sequelae of chronic administration of the drug. Periods of hyperactivity and increased wakefulness were observed in all cats receiving para-chlorophenylalanine and were followed by episodes of perceptual disturbances, manifested by overreaction to slight sounds, fixed point staring, and episodes of looking around the room as though

watching some obscure object in the air. Behavioral changes associated with long term administration of para-chlorophenylalnine are similar to those associated with prolonged selective deprivation of rapid eye movement sleep in both cats and rats. 26 references.

57032
AUTHORS: Soehring, Klaus; Schuppel, Rainer.
ADDRESS: Institute of Pharmacology, Hamburg University, Hamburg, West Germany
TITLE: Interactions between alcohol and drugs.
SOURCE: In: Popham, R., Alcohol and alcoholism.
SOURCEID: Toronto, University of Toronto Press, 1970. 421 p. (p. 73-79).

The interactions between alcohol and drugs are discussed. The combination of alcohol, hypnotics, antiepileptic drugs, psychoactive drugs, INH and other monoamine oxidase blockers; antihistaminic drugs; oral antidiabetic drugs; opiates and synthetic drugs with morphine-like action; and the pyrazolones are discussed. Psychopharmacological experiments in animals and humans are reviewed, along with biochemical and pharmacological studies. 35 references.

58227
AUTHORS: Smith, Douglas E.; King, Melvyn B.; Hoebel, Bartley G.
ADDRESS: Department of Psychology, Princeton University, Princeton, New Jersey 08540
TITLE: Lateral hypothalamic control of killing: evidence for a cholinoceptive mechanism.
SOURCE: Science.
SOURCEID: 167(3919):900-901, 1970.

In rats that would not ordinarily kill mice, lateral hypothalamicinjection of crystalline carbachol, a cholinomimetric, elicited killing. Norepinephrine, amphetamine, serotonin and sodium salts were ineffective at the same site. Carbachol was ineffective when injected into the medial, dorsal or ventral hypothalamus. As additional evidence for a cholinoceptive mechanism, neostigmine elicited killing, and, in spontaneous killers, methyl atropine blocked it. The results indicate that the lateral hypothalamus contains a cholinoceptive component of an innate system that activates killing, and anticholinergic treatment can be used as a means of suppressing killing. Pharmacological manipulation of such a system could be used in treatment of pathological aggressive behavior. 10 references. (author abstract modified)

58349
AUTHORS: Horlington, M.
ADDRESS: Pharmacology Dept., Smith and Nephew Research Ltd., Gilston Park, Harlow, Essex, England
TITLE: Startle response circadian rhythm in rats: lack of correlation with motor activity.
SOURCE: Physiology and Behavior.
SOURCEID: 5(1):49-53, 1970.

Acoustic startle response magnitude in rats exhibits an age related circadian rhythm beginning at sexual maturity, rising to a peak between 70 and 100 days, and followed by a decline. At 90 days, the night startle response magnitude is over 90% greater than during the day. Night startle response latency is also significantly shorter at this age. Startle response magnitude did not correlate with motor activity when immature and mature animals were compared during day and night conditions. Amylobarbitone sodium (20mg/kg s.c.) causing a 50% reduction in motor activity at night, did not affect startle response magnitude, and this was also observed following a dose of dexamphetamine sulfate (1.0mg/kg s.c.) which caused a 36% increase in motor activity during the day. 26 references. (author abstract modified)

58382
AUTHORS: Feldstein, A.; Chang, F. H.; Kucharski, J. M.
ADDRESS: Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts 01545
TITLE: Tryptophol, 5-hydroxytryptophol and 5-methoxytryptophol induced sleep in mice.
SOURCE: Life Sciences (Oxford).
SOURCEID: 9(6):323-329, 1970.

Tryptophol, 5-hydroxytryptophol and 5-methoxytryptophol were found to induce sleep in mice. The onset of action was most rapid for tryptophol and 5-methoxytryptophol; 5-hydroxytryptophol had the slowest onset, probably due to difficulty of transport across the blood - brain barrier. Sleep times were shortest for tryptophol and 5-methoxytryptophol and longest for 5-hydroxytryptophol. The tryptophols or the corresponding aldehydes may play a role in physiological sleep mechanisms. 7 references. (author abstract modified)

58430
AUTHORS: Kulkarni, A. S.
ADDRESS: P.O. Box 10 (Dow Chemical Company), Zionsville, Indiana 46077
TITLE: Magnesium pemoline: specificity of effects on instrumental avoidance learning.
SOURCE: Behavioral Neuropsychiatry.
SOURCEID: 2(3-4):42-46, 1970.

The magnesium hydroxide complex of pemoline (2-imino-5-phenyl-4-oxazolindinone), a CNS stimulant, is reported to facilitate avoidance learning in the rat. Male Harlan-Wistar rats placed in a Skinner box and subjected to a conditioned stimulus (CS) were used to separate the effect of Mg-Pem on learning from motor activity or from a nonspecific stimulation. The rats, 30 minutes after administration of 5mg/kg i.p. Mg-Pem, were subjected to 700 tests of a 15 second CS and avoidance acquisition responses were recorded using a printout counter. Twenty four hours after the original session, a retention session took place. Somatic motor activity (SMA) of the animals was measured for 1.5 hours. Results showed that improvement of the treated animals in avoidance responses was 70% over the control animal responses. The increment in learning of these animals at the end of the learning session was still present 24 hours later. Small, insignificant increases on wrong lever and incorrect responses were noted with Mg-Pem animals. SMA was increased in the drug treated group. The relationship of the increments revealed a definite increase in conditioned avoidance response (CAR) during the first hour with a slight increase in SMA. A leveling off in CAR with an increase in SMA appeared in the next half hour demonstrating that in instrument avoidance learning there is a dissociation between CAR and SMA. 29 references.

58492
AUTHORS: Freund, Gerhard.
ADDRESS: Department of Medicine, University of Florida, Gainesville, Florida 32601
TITLE: Impairment of shock avoidance learning after long-term alcohol ingestion in mice.
SOURCE: Science.
SOURCEID: 20(3):1599-1601, 1970.

Chronic alcohol consumption impaired the learning of a two way shuttle box avoidance task in mice 10 to 14 days after the discontinuation of ethanol in the diet. Control groups of 12 mice each received laboratory chow ad libitum or were pair fed with the alcohol consuming mice by diets containing isocaloric amounts of sucrose. The performance of the two control groups was indistinguishable from each other, and only the ethanol consuming mice performed poorly. It was therefore concluded that alcohol consumption per se and not a nutritional deficiency was responsible

for the impairment of learning. It may be that ethanol or its metabolites impair associative processes of learning in the central nervous system. 14 references. (author abstract modified)

58531
AUTHORS: Kornetsky, Conan; Eliasson, Mona.
ADDRESS: Division of Psychiatry, Boston University School of Medicine, Boston, Massachusetts
TITLE: Reticular stimulation and chlorpromazine: an animal model for schizophrenic overarousal.
SOURCE: Science.
SOURCEID: 165(3899):1273-1274, 1970.

Certain schizophrenic patients are in a state of continual central excitation and improvement in these patients after treatment with chlorpromazine is a result of the action of the drug in reducing this excitation. An "inverted U" model was developed to test this postulated state of central excitation. Three rats were electrically stimulated in the mesencephalic reticular formation while performing a simple attention task. Stimulation or treatment with chlorpromazine impaired the performance of the animals; however, the two treatments together resulted in performance indistinguishable from that seen after injections of saline alone. 9 references. (author abstract modified)

58840
AUTHORS: Reis, Donald J.; Moorhead, Dudley T., II; Merlino, Nancie.
ADDRESS: Dept. of Neurology, Cornell University Medical College, New York, N. Y. 10021
TITLE: Dopa-induced excitement in the cat: its relationship to brain norepinephrine concentrations.
SOURCE: Archives of Neurology.
SOURCEID: 22(1):31-39, 1970.

Adult cats were used to study the effect of L-dopa on brain norepinephrine levels. Within 45 minutes of administration, L-dopa (20mg/kg) produced a striking state of excitement in cats pretreated with pheniprazine hydrochloride (20mg/kg). The evoked behavior was similar to sham rage in which features of flight predominated. Neither L-dopa nor pheniprazine in this dosage by itself produced any change in behavior. Pretreatment with reserpine (0.75mg/kg i.p.) did not attentuate the L-dopa induced excitement, but it did shorten the latent period to the onset of the behavior. Prior treatment with disulfiram (300-500 mg/kg i.p.) markedly attenuated the L-dopa induced behavior after pheniprazine and reserpine. The concentration of norepinephrine in the lower brain stem was slightly increased by L-dopa alone and unchanged by pheniprazine. It was markedly increased by L-dopa after pheniprazine treatment whether or not reserpine or disulfiram was present. There was a high level of correlation between norepinephrine levels in the brain stem and the magnitude of excitement in individual cats receiving the above drugs alone or in combination. The release of norepinephrine by adrenergic neurons in the brain probably triggers sham rage behavior in the cat. 62 references. (author abstract modified)

51782
AUTHORS: U. S. House Committee on Government Operations.
ADDRESS: Washington, D. C.
TITLE: The British drug safety system.
SOURCEID: Washington, D. C., U. S. Govt. Printing Office, 1970. 100 p. 45 cents.

A report on the British Drug Safety System as prepared by the Committee on Government Operations of the 91st Congress of the United States is presented. Aspects considered in this report include the following: the British and American drug systems in perspective, origins and characteristics of the British drug safety system, thalidomide and the British reaction, the development of the voluntary system during 1964, the movement toward comprehensive drug legislation, the Government's Medicines Bill, the debate in Parliament, and implementation of the statutory system. The responsibilities of Britain's Committee on the Safety of Drugs include the following: to invite from the drug manufacturer any necessary reports on thetoxicity tests carried out on the drug; to obtain reports of clinical trials of drugs submitted; to consider whether the drug may be released for marketing, with or without precautions or restrictions on its use; to give manufacturers and others concerned any necessary advice; and to assemble and assess reports about the adverse effects of drugs.

55323
AUTHORS: Abbs, E. T.; Robertson, M. I.
ADDRESS: Dept. of Pharmacology, School of Pharmacy, Portsmouth Polytechnic, Portsmouth, England
TITLE: Selective depletion of noradrenaline: a proposed mechanism of the adrenergic neurone-blocking action of bretylium.
SOURCE: British Journal of Pharmacology (London).
SOURCEID: 38(4):776-791, 1970.

A study is presented of the effects of bretylium on the content and subcellular distribution of norepinephrine in cat spleen and on the overflow of norepinephrine in response to stimulation of the splenic nerve. Bretylium, 15 minutes after its administration, produces a significant depletion of norepinephrine in only the supernatant fraction of homogenate, an adrenergic neuron blockade being evident. This depletion is apparent up to 18 hours later, but disappears 7 days later, when nerve function is also restored. Both these developments are prevented by prior administration of (+)-amphetamine. In bretylium pretreated cats, the norepinephrine content of the supernatant fraction is replenished and the neuron blockade abolished after treatment with (+)-amphetamine. The depletion of norepinephrine, evident after treatment with bretylium, appears to be unassociated with adrenergic neuron blockade. It is concluded that bretylium produces its adrenergic neuron blocking activity by depleting norepinephrine from a store whose amine appears in the supernatant fraction after homogenization. 18 references. (author abstract modified)

55398
AUTHORS: Zitkova, L.; Stastna, J.; Celikovska, G.; Kurti, V.
ADDRESS: Tuberkulose-Forschungsinstitut, Prague 8 - Bulovka, Czechoslovakia
TRTITLE: /Liver damage following application of pyrazinamide in animal experiments: 1. changes in body weight of rats under the influence of pyrazinamide./
TITLE: Leberschadigung nach Verabreichung von Pyrazinamid im Tierversuch: 1. Anderungen des Korpergewichtes von Ratten unter Einwirkung von Pyrazinamid.
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 20(1):151-153, 1970.

The effect of a daily dose of 3gm/kg pyrazinamide on food intake

and body weight of rats was examined over a period of 1 week. The substance was administered by stomach tube in a 10% solution of acacia gum: a control group received 10% acacia gum solution. After 7 days, the pyrazinamide group showed a 27% decrease in food intake as compared to that of the controls, and a significant (11%) reduction of body weight. Loss of body weight in the control group over the same period was only 3%. 12 references. (author abstract modified)

57605
AUTHORS: Robson, J. M.
ADDRESS: Chelsea College of Science and Technology, London, England
TITLE: Testing drugs for teratogenicity and their effects on fertility; the present position.
SOURCE: British Medical Bulletin (London).
SOURCEID: 26(3):212-216, 1970.

Methods for detection of drugs producing congenital abnormalities are essentially empirical and consist of administering drugs at various dose levels to animals and examining fetuses not only by the naked eye, but also for soft tissue and bony anomalies. Investigations on the metabolism and elimination of drugs, as well as on the passage of these drugs and their metabolities into the embryo, should utlimately form an essential part of these studies. There is good evidence that a variety of mechanisms by which drugs produce their embryotoxic and teratogenic effects are involved with different drugs. Examples are inhibition of mitotic processes with aminopterin, or the effective level of the hormone necessary for the maintenance of normal pregnancy, or insufficient blood and oxygen supply to the embryo. Much more basic work on the mechanisms of action of drugs is necessary. Some recent studies show that LSD is a teratogen and can also interfere with fertility. Malformations were also produced by mescaline and 2-bromo-LSD (BOL 148). All 3 drugs caused an increase in resorption and fetal mortality. There are also a number of reports of LSD producing various types of damage to chromosomes, both in vitro and in vivo. There is evidence that 1 form of cannabis (ganja) can produce serious teratogenic effects when administered to rats. Studies of 2 chemical defoliants are also described. 15 references.

57606
AUTHORS: Hanley, T.; Udall, V.; Weatherall, M.
ADDRESS: Wellcome Foundation Ltd., London, England
TITLE: An industrial view of current practice in predicting drug toxicity.
SOURCE: British Medical Bulletin (London).
SOURCEID: 26(3):203-207, 1970.

Before a new substance is administered to man, as much evidence as possible is needed about its potential hazards. Such evidence can be obtained at present only from experiments in animals. Recommended tests include observations on acute pharmacodynamic effects in convenient mammalian species, and measurement of the oral and parenteral LD50 in rats or mice, based on the mortality within 1 day and within 1 week. Assessment of toxicity over longer periods is based on daily administration. Studies on fertility, teratogenicity, carcinogenicity, local toxicity, and interactions with other agents are additional requirements. Once the decision to use the drug in man has been made, the investigation will usually go ahead in successive stages, which increase in scale as the accumulated experience generates confidence. When the therapeutic action of the new drug has been solidly established, the question of whether or not to market the drug arises. It seems likely that there will always be a small element of toxicity that cannot be predicted until human beings are exposed to the drug on a very large scale. Prediction of toxicity should depend on the judgement of an independent authority, at the national or international level. 19 references.

57607
AUTHORS: Baker, S. B. de C.; Davey, D. G.
ADDRESS: Imperial Chemical Industries Ltd., Pharmaceuticals Division, Alderley Park, Macclesfield, Cheshire, England
TITLE: The predictive value for man of toxicological tests of drugs in laboratory animals.
SOURCE: British Medical Bulletin (London).
SOURCEID: 26(3):208-211, 1970.

It is known that a wide range of chemicals can produce tumors in animals. Drugs that have an obvious carcinogenic effect as on mitosis or tumor development with little or no preliminary changes are clearly unacceptable. Drugs which produce tumors clearly secondary to other lesions may be regarded as safe provided the therapeutic use does not produce the lesion. The liver is probably the most vulnerable organ in the body for the exhibition of drug toxicity. The principle reaction to toxins is necrosis and functional changes giving rise to jaundice. The prediction of jaundice in man from animal experimentation, however, is particularly difficult. Liver enlargement is frequently found in animals and can be produced by drugs known to be safe in man. Toxic reactions may bring damage to sensory organs and are admittedly worrying to the laboratory toxicologist. Idiosyncratic reactions probably arise, in most instances, from sensitization. One of the worst offending drugs is penicillin. Reactions arising from pharmacogenetic differences within a species would be detected in a laboratory study only by chance. It is the task of the toxicologist to try to foresee what other drugs might be used with the candidate drug so that he can test for interaction. Within the limitations discussed, it is believed that good laboratory work makes the risk of new drugs small. 11 references.

58572
AUTHORS: Mork, David P. S.; Kessler, Wayne V.; Shaw, Stanley M.
ADDRESS: Department of Biology, Saint Cloud State College, Saint Cloud, Minnesota 56301
TITLE: Placental transfer of pentobarbital in the rat.
SOURCE: Journal of Pharmaceutical Sciences.
SOURCEID: 59(6):803-805, 1970.

The placental transfer of pentobarbital and/or metabolites was determined in rats using 14C-labeled pentobarbital. The level of pentobarbital and/or metabolites in fetal blood was greatly influenced by the circulating level of pentobarbital and/or metabolites in the mother. Of the total pentobarbital and/or metabolites transferred, the percentage of unbound pentobarbital in fetal blood plasma was influenced by the pentobarbital dose level administered to the pregnant rat. A greater percentage of total pentobarbital and/or metabolites was present as unbound pentobarbital in fetal blood plasma than in maternal blood plasma. Chronic administration of pentobarbital during gestation decreased sensitivity to the pharmacological effects of further drug administration to the newborn. The changes induced by pretreatment were not permanent. 10 references. (author abstract)

51651
AUTHORS: Morrison, Cathleen F.
ADDRESS: Tobacco Research Council Laboratories, Harrogate, England
TITLE: A potential screening test for minor tranquillizing drug action.
SOURCE: British Journal of Pharmacology (London).
SOURCEID: 38(2):460P, 1970.

A screening test for minor tranquilizing drug action is described which employs a Y-maze with 1 open-sided arm. Rats treated with minor tranquilizers (30mg/kg chlordiazepoxide) and sedatives (15mg/kg amobarbital) show a greater tendency to explore the open-sided arm than do untreated rats, who ordinarily tend to avoid that arm. Effects of other centrally active drugs such as chlorpromazine, imipramine and atropine are not detectable by this test. The Y-maze has advantages over punished behavior as a screening test for drugs similar in action to chlordiazepoxide since no complex equipment is required and results can be obtained quickly using untrained animals. 3 references.

58357
AUTHORS: Altaffer, Fred B.; De Balbian Verster, F.; Hall, Scott; Long, Charles J.; D'Encarnacao, Paul.
ADDRESS: Department of Psychology, Wisconsin State University, Eau Claire, Wisconsin 54701
TITLE: A simple and inexpensive cannula technique for chemical stimulation of the brain.
SOURCE: Physiology and Behavior.
SOURCEID: 5(1):119,121, 1970.

A simple, inexpensive, rapid, and accurate method for chemical stimulation of both dorsal and ventral structures in the brain utilizes a cannula made from polyethylene tubing. An anchoring bulb is formed near one end by application of heat, and the other end is sealed. Implantation of large dorsal structures is easily done without the use of a stereotaxic instrument; once the cannula is in place, intracerebral administration of chemicals is made by cutting off the sealed end, inserting a microsyringe, and resealing the tip. For deep lying or ventral structures, a combination of stainless hypodermic needle tubing and polyethylene tubing is used. Animals implanted with this type of cannula have been used for several months with minimal loss due to blockage or damage to the cannula. Detailed illustration of the device is provided. 4 references.

58358
AUTHORS: Wadler, Ronald D.
ADDRESS: Dept. of Psychiatry, State University of New York, Downstate Medical Center, Brooklyn, N. Y.
TITLE: An improved instrument for implanting micropellets in the brain.
SOURCE: Physiology and Behavior.
SOURCEID: 5(1):123-124, 1970.

Implantation of micropellets of chemical agents in animal brains may be accomplished with an instrument constructed from a 1 cc syringe, a stylus, and a 26 gauge hypodermic needle cut flat at the tip. The stylus is used to tamp a substance into a micropellet within the needle, which may then be attached to the vertical drive of a stereotaxic instrument for implantation of the micropellet within brain tissue. This technique makes possible accurate intracerebral implantation of chemicals without attaching cannulas to the skull. A detailed illustration of the device is provided. 8 references. (author abstract modified)

06 METHODS DEVELOPMENT
58880

AUTHORS: Patterson, D. A.; Stevens, H. M.
ADDRESS: Home Office Central Research Establishment, Aldermaston, Reading, Berkshire, England

TITLE: Identification of cannabis.

SOURCE: Journal of Pharmacy and Pharmacology (London).
SOURCEID: 22(5):391-392, 1970.

A procedure is described for analysis of cannabis that is advantageous in combining 2 independent techniques for the detection of 3 cannabis components and which offers positive identification in a reasonably short time. It consists of extraction of the suspected cannabis or cannabis resin sample with a stock solution of dibenzylphthalate in light petroleum, the extract then being analyzed, without further purification, by gas chromatography or by paper chromatography. 7 references.

07 EARLY CLINICAL DRUG TRIALS

57483
AUTHORS: Johnson, A. W.
ADDRESS: Veterans Administration Hospital, Danville, Ill.
TITLE: One pill for two.
SOURCE: Newsletter for Research in Psychology.
SOURCEID: 12(2):30-33, 1970.

Sinequan (doxepin hydrochloride) was administered to self-care psychiatric patients who were receiving concomitant antidepressant and ataractic medication. Twenty eight patients were placed exclusively on Sinequan (25mg, 3 times daily) for 30 days. All subjects were rated using the intropunitive anxiety scale and a depressive mood scale. For subjects who completed the study, Sinequan was no less effective than the double medication. It is also likely that subjects who withdrew from the study may have suffered withdrawal symptoms when prior medication was discontinued, and that Sinequan was ineffective in managing resultant discomfort. 3 references.

57608
AUTHORS: Mansel-Jones, D.
ADDRESS: Committee on Safety of Drugs, London, England
TITLE: The role of the Committee on Safety of Drugs.
SOURCE: British Medical Bulletin (London).
SOURCEID: 26(3):257-289, 1970.

The Committee on Safety of Drugs began operation in 1964 in the United Kingdom and has demonstrated the successful operation of a review system of drug safety, based on voluntary arrangements and possessing no legal power. The major concerns are chemistry, pharmacodynamics, metabolism, toxicity involving acute and intermediate term studies, teratology, and drug interaction. In examining the outline of a proposed clinical trial, the Committee wishes to be satisfied that staff and facilities are appropriate to the early study of the drug. Data are expected from detailed hematological and clinical chemistry monitoring in patients during clinical trials. Evidence of biological availability is presented, major clinical drug interaction problems should have been clarified, and problems such as possible capricious absorption solved. The proposed promotional literature which will be made available to doctors is examined in broad outline. The primary mechanism for monitoring drugs after marketing is based on a voluntary reporting system for suspected adverse reactions. The Committee is charged with operating an early warning system, drawing attention to unfamiliar or previously undocumented hazards. 1 reference.

58281
AUTHORS: Spiegelberg, U.; Petrilowitsch, Nikolaus.
ADDRESS: Univ.-Nervenklinik, 355 Marburg/Lahn, Ortenbergstrasse 8, Germany
TRTITLE: /Dimethacrine -- a new tricyclic antidepressant: open investigations in a clinic and polyclinic./
TITLE: Dimetacrin -- ein neues trizyklisches Antidepressivum: offene Erkundungsuntersuchungen in Klinik und Poliklinik.
SOURCE: Medizinische Welt (Stuttgart).
SOURCEID: 21(6):227-230, 1970.

The clinical testing of a new tricyclic antidepressant, dimethacrine (9,9-dimethyl-10-(3-dimethylaminopropyl)acridan), is presented. It was tested in 60 patients (36 ambulant, 24 hospitalized) for its effects on anxiety and depression. Within 4 weeks, it was shown to be effective in 58.33% of the total cases. Of the 27 endogenous depressions, 66.67% improved; of the 13 involutional depressions, 69.28% improved; and for the total depressive cases, the improvement was 67.50%. On a daily dosage of 75-300mg i.m., local and general tolerance was good. The side effects appeared of slight consequence. 26 references. (author abstract modified)

58373
AUTHORS: Yaryura-Tobias, Jose A.; Wolpert, Arthur; White, Leonard; Agola, Pietro; Merlis, Sidney.
ADDRESS: Research Division, Central Islip State Hospital, Central Islip, New York.
TITLE: A clinical evaluation of clopenthixol.
SOURCE: Current Therapeutic Research.
SOURCEID: 12(5):271-279, 1970.

Fifty eight adult female chronic schizophrenic patients with at least 3 years of continuous hospitalization and no other major illnesses were studied for 20 weeks. (A double-blind procedure was not used.) Clopenthixol was started at 25mg twice daily for one week and increased until therapeutic effects or a maximum daily dose of 300mg was reached. Statistical analysis showed symptomatic improvement in conceptual disorganization, tension, mannerisms, depressive mood, excitement and hostility. Some improvement also was noted in emotional withdrawal, cooperativeness, anxiety, guilt and hallucinations, although a high dose could elicit hallucinations. Side effects included hypotension, tachycardia, parkinsonian symptoms and drowsiness. Clopenthixol appears to be an antipsychotic agent having clinical properties similar to those of the phenothiazines. 9 references.

58374
AUTHORS: Gershon, Samuel; Hekimian, Leon J.; Burdock, Eugene I.; Kim, Suk Sik.
ADDRESS: Department of Psychiatry and Neurology, New York University Medical Center, 550 First Avenue, New York 10016
TITLE: Antipsychotic properties of loxapine succinate.
SOURCE: Current Therapeutic Research.
SOURCEID: 12(5):280-285, 1970.

Ten acute schizophrenics (5 men and 5 women) were treated for 3 to 4 weeks (mean - 23 days) with loxapine succinate in daily doses ranging from 20-100mg (mean maximal daily dose, 56.5mg). All patients showed extrapyramidal side effects, with the women tolerating higher doses than the men. Only 3 out of 10 patients treated were able to be discharged from the hospital; 5 of the 10 were given a rating of moderate improvement at the termination of treatment. The compound appears to be most effective on the symptoms of anger, hostility and hallucination and improves manageability. However, overall antipsychotic effects are not convincing and seem to be inferior to chlorpromazine. Particularly striking in this study was the observation that, although this compound produced marked extrapyramidal side effects, these did not parallel its antipsychotic activity. Clinically, loxapine might have some usefulness against the target symptoms of anger and hostility. 9 references. (author abstract modified)

58456
AUTHORS: Robie, Theodore R.
ADDRESS: 6 Brookwood Drive, Montclair, New Jersey
TITLE: Crash treatment for melancholia resistant to other recently developed methods.
SOURCE: Journal of the Medical Society of New Jersey.
SOURCEID: 67(8):488-493, 1970.

Antidepressant chemotherapy has largely replaced electrophysiologic treatment of melancholia. To facilitate recovery as quickly as possible, and to establish hope for the complete remission of symptoms, an effort was made to intensify dissemination of serotonin (5-HT) by introducing 5-hydroxytryptophan i.v., then converting it into 5-HT by parenteral injection of methyl phenidate (Ritalin). It was seen that this intensification could be accomplished with any one of the monoamine oxidase (MAO) inhibitors

administered orally, three times a week. Any patient that does not progress satisfactorily on thymoleptic antidepressants (Imipramine, Elavil, Norpramine, Aventyl, or Pertofrane) should stop medication; and, after a 3 day interval with no chemotherapy other than oral Ritalin, the patient should be placed on MAO inhibitor therapy. A week or 2 later the patient can be started on the intensified serotonin regime, and in a short period good remission can be expected. Although many successes were evident with (MAO) inhibitors or cyclothymics, there were some unsatisfactory results. Hyperpyrexia and sometimes death may occur if patient medication is changed from MAOI to thymoleptic chemicals, and vice versa.

56500
AUTHORS: Ramsay, R. A.; Ban, T. A.; Lehmann, H. E.; Saxena, B. M.; Bennett, Jean.
ADDRESS: Allan Memorial Institute, 1025 Pine W., Montreal, Quebec, Canada
TITLE: A comparative study of molindone and trifluoperazine.
SOURCE: Current Therapeutic Research.
SOURCEID: 12(7):438-440, 1970.

The therapeutic effectiveness of molindone, an oxygenated indole compound, was compared with the standard trifluoperazine in a 12-week double-blind study of 20 chronic schizophrenic patients. Both drugs were administered orally; dosages of 20mg/day of molindone or 60mg/day of trifluoperazine were attained by the eighth week and maintained thereafter. Comparison of the two drugs was based on a Brief Psychiatric Rating Scale (BPRS) of anxiety, tension, suspiciousness; a Nurses' Observation Scale for Inpatient Evaluation (NOSIE); a Clinical Global Impression; and on the occurrence of clinical side-effects or abnormal measurements of pulse, blood pressure and weight as measured by Treatment Emergent Symptom. On the BPRS, trifluoperazine showed a significant difference (P less than 0.05) in tension evaluation. In social competence and social interest on the NOSIE, the standard drug revealed statistically significant differences. An improvement trend in retardation was noted with molindone in this evaluation. No significant differences were noted between either drug in the Clinical Global Impression. Both the standard and investigational drug showed similar clinical side-effects of urinalysis, liver function and extrapyramidal reactions. Thus, no significant differences in the therapeutic effectiveness of the two drugs appeared in schizophrenic patients. 5 references.

58372
AUTHORS: Malm, Ulf.
ADDRESS: Department II, Lillhagen Mental Hospital, Box 3005, 422 03 Hisings-Backa 3, Gothenburg, Sweden
TITLE: Clothiapin in the treatment of chronic schizophrenia.
SOURCE: Current Therapeutic Research.
SOURCEID: 12(5):261-270, 1970.

Thirty chronic male, hospitalized schizophrenic patients were treated for an average of 8 months with a new nonphenothiazine compound, clothiapin, 2-chloro-11-(4-methyl-1-piperazinyl)-dibenzo-(b,f)(1,4)-thiazepine. When psychopathological target symptoms, Activities of Daily Living and Work Performance on the last day of treatment with clothiapin were compared with the same parameters on the last day of treatment with previous psychotropic drugs, 9 patients were estimated to have improved, 15 patients were unaltered and 4 patients deteriorated, while 2 patients did not complete the investigation. The most important side effects were of the extrapyramidal type. The results indicate that clothiapin is suitable as a basic major tranquilizer for both acute antipsychotic use and in maintenance treatment in connection with rehabilitation. 8 references. (author abstract modified)

52483
AUTHORS: Kessell, A.; Pearce, T. A. A.; Holt, N. F.
ADDRESS: Dandenong Psychiatric Centre, Victoria, Australia
TITLE: A controlled study of nortriptyline and imipramine.
SOURCE: American Journal of Psychiatry.
SOURCEID: 126(7):938-945, 1970.

A double-blind comparison was made of the secondary amine, nortriptyline, and the tertiary amine, imipramine, in female outpatients with a primary depressive illness. There was no significant difference in the overall response between the two drugs, although other differences were found. It was not possible to confirm clinically the hypothesis that the action of the tertiary amines is medicated through secondary amine derivatives and that tertiary amine configuration is associated with tranquilization and secondary amine configuration with thymoleptic activity. 4 references. (Author abstract)

55738
AUTHORS: Hofmann, K. W.; Manach, J.; Sogtrop, H. H.
ADDRESS: Centre de Recherches CLIN-BYLA, Paris, France
TRTITLE: /Dipotassium chlorazepate: clinical reports on a new antianxiety agent./
TITLE: Dikalium-chlorazepat: Klinische Berichte uber ein neues Anxiolyticum.
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 20(1):130-137, 1970.

A review of clinical reports concerning dipotassium chlorazepate (CB-4306, Tranxilium) published in various French journals is presented. In general, the drug was applied in cases of stubborn depression. It was well tolerated, the chief side-effect being somnolence. Results were regarded as satisfactory in most cases. A brief discussion of the effect of CB-4306 on driving competence indicates that the drug did not affect simple visual reaction time, nor did it significantly affect braking time. It reduced the chance for successful negotiation of a narrow passage. Judgment of speed was not significantly affected. 17 references.

58375
AUTHORS: Dyson, William L.; Barcai, Avner.
ADDRESS: Department of Psychiatry, University of Pennsylvania, Philadelphia, Pa. 19104
TITLE: Treatment of children of lithium-responding parents.
SOURCE: Current Therapeutic Research.
SOURCEID: 12(5):286-290, 1970.

There is evidence indicating that manic depressive children of lithium-responding parents will also respond, as there may be a hereditary factor involved in manic-depressive illness. Two detailed cases of children treated first with amphetamine, then with lithium carbonate, reveal positive changes in behavior and performance. After 6 weeks of lithium carbonate at 1500mg/day, manic depressive symptoms decreased, attention span increased, and several phobias in onesubject were relieved. When medication was discontinued, all earlier symptoms reappeared. 6 references.

58431
AUTHORS: Marshall, Myron H.
ADDRESS: Author address not given
TITLE: Are there "benefits" of mental illness?
SOURCE: Behavioral Neuropsychiatry.
SOURCEID: 2(3-4):40-42, 1970.

Hypercompetency and heightened creativity, have been observed in patients in the high phases of cyclothymic disorders. Limited

observations of paranoids suggest that the degree of hypercompetency is a direct result of the mental illness, thus a "benefit" of the illness itself. The association of creativity and psychiatric illness has been recognized by American industry, which effectively motivates a creative person who may otherwise have an "odd" personality. Examples from the literature of mental illness in very creative individuals are briefly reviewed. Although the neurotic conflict is not associated with creativity in all persons, it may act as a stimulant to the creative process. Drugs or therapy may remove this disorder along with its "benefit". Instruments for the subjective or objective rating of the effects of lithium on creativity are currently being designed. Early observations reveal that lithium, while controlling the mood swings of manic-depressives, alters the creative process, thus removing the "benefit" of the mental illness. 17 references.

52456
AUTHORS: Klerman, Gerald L.; Gershon, Elliot S.
ADDRESS: Department of Psychiatry, Yale University School of Medicine, 34 Park Street, New Haven, Connecticut 06519
TITLE: Imipramine effects upon hostility in depression.
SOURCE: Journal of Nervous and Mental Disease.
SOURCEID: 150(2):127-132, 1970.

A reciprocal relationship between hostility and depression is postulated by psychodynamic theory. Following the classic formulations derived from Freud and Abraham, the turning of hostility away from the object world and onto the ego is a crucial mechanism in the psychogenesis of depression. The effects of imipramine and other antidepressants have been studied for possible verification of this hypothesis. Based on clinical observations and research studies, it is postulated that imipramine mobilizes hostility and that this mobilization underlies the drug's therapeutic psychodynamic action. In a study of psychodynamic changes in women with depression, opportunity was afforded to test this view. Three women, hospitalized for their depressions, were studied longitudinally before and during treatment with imipramine. Using the Gottschalk verbal sample technique, hostility directed inward and directed outward was measured. No significant differences were found between the imipramine and preimipramine periods, despite significant clinical improvement during the drug treatment period. Further longitudinal studies of the effects of imipramine upon hostility are needed, before the "mobilization hypothesis" can be accepted or dismissed. 24 references. (Author abstract)

52574
AUTHORS: Cadden, James J.; Flach, Frederic F.
ADDRESS: Cornell University Medical School, 1300 York Avenue, New York, New York 10021
TITLE: Differential response to treatment as a function of the changing character of a depression.
SOURCE: American Journal of Psychiatry.
SOURCEID: 126(7):1013-1016, 1970.

The proper choice of an antidepressant in a given clinical situation is often controversial. The differential response to treatment as a function of the changing character of a depression must be considered. The case presented points up the necessity for viewing each episode of a recurrent depressive illness in terms of both the psychopathology and the psychodynamics before choosing a therapeutic agent. Current thinking on the use of antidepressant medications is reviewed. 13 references. (Journal abstract modified)

55689
AUTHORS: Schuffel, Wolfram; Schaumburg, Cornelia; Schafer, Nikolaus.
ADDRESS: Abteilung fur Psychosomatik und Psychoterapie des Zentrums fur Innere Medizin der Universitat, 79 Ulm, Steinhovelstrasse 9, Germany
TRTITLE: /The psychopharmacological treatment of cardiac neurotic patients with dipotassium chlorazepate in the double-blind test./
TITLE: Die psychopharmakologische Behandlung des Herzneurotikers mit Dikalium-chlorazepat im Doppelblindversuch.
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 20(1):127-130, 1970.

Dipotassium chlorazepate (TR-19119) was given in a double-blind experiment to 67 cardiac neurotic patients, and their responses were observed during a 3 week period. A battery of psychological tests was given before the experiment was run and again at the conclusion. These included the Hamburg - Wechsler adult intelligence test, the Cattell objective analytic anxiety battery, Beck's depression inventory, the Beckmann - Zenz scale of somatic complaints, Rorschach

Test, Object Relations test, and Minnesota Multiphasic Personality Inventory (MMPI). There were not significant differences between findings related to patients who received dipotassium chlorazepate and the placebo patients, with the exception of the Beckmann - Zenz scale of somatic complaints, in which there was a significant drop in the drug treated group. 14 references. (author abstract modified)

58335
AUTHORS: Tyson, V.
ADDRESS: Author address not given
TITLE: Two trials with a new psychotherapeutic drug in the treatment of anxiety.
SOURCE: The Practitioner (London).
SOURCEID: 204(1220):306-309, 1970.

A double - blind, between - patient comparison of oxypertine (Integrin) and placebo was made on 50 patients for 2 weeks (30mg/day). In a second trial, a double -blind, cross - over comparison was made between oxypertine (20mg thrice daily) and placebo, for 2 weeks. 30mg/day dose was found inadequate for most of the patients, suffering from a moderately severe anxiety neurosis; the 60mg/day dose was superior to placebo. Incidence of side effects was high in both trials, the main complaint being sedation. 1 reference.

58404
AUTHORS: Carroll, B. J.; Mowbray, R. M.; Davies, Brian.
ADDRESS: Department of Psychiatry, University of Melbourne, Royal Melbourne Hospital, Victoria 3050, Australia
TITLE: L-tryptophan in depression.
SOURCE: Lancet (London).
SOURCEID: No. 7658:1228, 1970.

As reported previously, L-tryptophan was not found to have antidepressant properties in comparison to electroconvulsive therapy. Others have reported L-tryptophan as effective an antidepressant as imipramine. It is suggested that comparison with an inert substance is necessary in the assessment of antidepressant drugs. It isurged that the therapeutic properties of L-tryptophan be stringently tested and reported with caution.

52455
AUTHORS: Karp, Stephen A.; Kissin, Benjamin; Hustmyer, Frank E., Jr.
ADDRESS: Department of Psychology, George Washington University, Washington, D. C.
TITLE: Field dependence as a predictor of alcoholic therapy dropouts.
SOURCE: Journal of Nervous and Mental Disease.
SOURCEID: 150(1):77-83, 1970.

The present study was designed to investigate relationships between perceptual field dependence and selection criteria and dropout rates for alcoholic outpatients assigned to psychotherapy and drug therapy programs. Nineteen selectees for individual "insight" psychotherapy were compared with 19 nonselectees and with 18 drug therapy patients. On the basis of prior studies of field dependence it was hypothesized that alcoholics selected, by traditional clinical criteria, for insight psychotherapy would be significantly more field-independent than nonselectees. This hypothesis was supported by the results. It was further hypothesized that field dependence would be related to dropout status of alcoholic patients. Relatively field-dependent patients were expected to be early dropouts from psychotherapy, and relatively field-independent patients were expected to be early dropouts from drug therapy. The present results suggest that early dropouts from psychotherapy are significantly more field-dependent than remainers. However, no differences in field dependence were obtained between dropouts and remainers in drug therapy. 10 references. (Author abstract)

52476
AUTHORS: Bowen, William T.; Soskin, Robert A.; Chotlos, John W.
ADDRESS: Veterans Administration Hospital, 2200 Gage Boulevard, Topeka, Kansas 66622
TITLE: Lysergic acid diethylamide as a variable in the hospital treatment of alcoholism: A follow-up study.
SOURCE: Journal of Nervous and Mental Disease.
SOURCEID: 150(2):111-118, 1970.

The use of lysergic acid diethylamide (LSD) in the treatment of alcoholism has led to many claims as to the drug's efficacy, but without a controlled study of both inhospital application and posthospital adjustment of patients. The present paper is concerned with the use of LSD in placebo and maximum dosages as a concomitant of a human relations training laboratory treatment program. Patients receiving LSD were also compared with patients completing the laboratory program but not receiving LSD. Findings were such as to indicate that the long term gains through use of LSD are negligible. A successful posttreatment adjustment seems more closely associated with pretreatment employment level, marital status, and whether or not the patient completes the treatment program. 14 references. (Author abstract)

54890
AUTHORS: Chosy, Julius J.; Lewis, William C.; Graham, David T.
ADDRESS: Univ. of Wisconsin Medical School, 1300 University Ave., Madison, Wis. 53706
TITLE: Phobia questionnaire responses and urine catecholamines.
SOURCE: Archives of General Psychiatry.
SOURCEID: 22(1):58-62, 1970.

An objective self administered test was used in an attempt to define the relationship of urine catecholamines to 2 subdivisions of anxiety. The specific aim was to find, in urine epinephrine and norepinephrine excretion, a chemical distinction that paralleled the psychological distinction between separation and body harm anxiety. For the psychological classification, the test instrument used was a list of 26 items referring to various phobias. The test was given to entering university freshmen, National Guardsmen, and to psychiatric

outpatients. Aliquots of the urine samples were acidified to pH 2.5 to 3.0 with hydrochloric acid, and frozen. Free epinephrine and norepinephrine were measured by chromatography. The hypotheses was not supported by the data since no difference in epinephrine/norepinephrine ratio or absolute excretion values was found in relation to the separation and body harm phobias. The study does suggest, however, that in a more general way, groups of subjects who are differentiated on the basis of an objective paper and pencil test can also be differentiated by their urinary epinephrine excretion. 31 references.

55393
AUTHORS: Zappoli, R.; Papini, M.
ADDRESS: Nervenklinik der Universitat Florenz, Institut fur Diagnose und Therapie der Epilepsien, Via S. Salvi 12, Florence, Italy
TRTITLE: /Therapy of partial epilepsy with a combination containing sultiamum./
TITLE: Die Behandlung der partiellen Epilepsien mit einer Sultiamum enthaltenden Kombination.
SOURCE: Arzneimittel-Forschung (Wurttemberg).
SOURCEID: 19(12):2001-2007, 1970.

Various forms of partial epilepsy in 64 patients were treated with a compound that combined N-(4'-sulfamylphenyl)-butanesultam-1,4 and diphenylhydantoin, N-methylethylphenylbarbituric acid and caffeine. Seizure frequency was reduced more than 50% in 70.3% of the cases. The effect did not diminish over an average period of administration of more than 23 months. The drug is especially effective in focal epilepsy. 14 references. (author abstract modified)

56574
AUTHORS: Cotzias, George C.; Papavasiliou, Paul S; Fehling, Clas; Kaufman Barry; Mena, Ismael.
ADDRESS: Medical Dept., Brookhaven National Laboratory, Upton, New York 11973
TITLE: Similarities between neurologic effects of L-dopa and of apomorphine.
SOURCE: New England Journal of Medicine.
SOURCEID: 282(1):31-33, 1970.

The effects of subcutaneous administration of apomorphine were studied in 15 patients with selected neurological disorders. Apomorphine injections were followed by unexpected dizziness, faintness, sleepiness, hypotension, bradycardia, and on 2 occasions, brief syncope, ranked in diminishing frequency. The patients with dystonia musculorum deformans, hemiplegia, and one with Parkinsonism who had not yet received L-dopa showed no diminution in neurologic scores. Patients suffering from Parkinsonism who showed improvement from L-dopa showed similar improvements with apomorphine. The results indicate that the short-lived neurologic effects of apomorphine tendered to duplicate the sustained therapeutic effects of L-dopa. The responses to apomorphine may improve to be less pronounced before L-dopa than after the chronic administration of this compound.

56779
AUTHORS: Nathan, P. W.
ADDRESS: Medical Research Council, National Hospital for Nervous Diseases, Queen Square, London, W.C.1, England
TITLE: The action of diazepam in neurological disorders with excessive motor activity.
SOURCE: Journal of the Neurological Sciences (Amsterdam).
SOURCEID: 10(1):33-50, 1970.

Diazepam was given intravenously (20mg) to 13 patients with various neural disorders characterized by abnormal and excessive

motility. Resting and spontaneous motor unit activity was abolished; tone was reduced. Tendon jerks were rendered normal; clonus and the flexor reflex remained. There was a reduction or abolition of the spread of reflex movements. In many conditions reciprocal innervation returned to some extent. The effect of diazepam in stopping or reducing excessive and abnormal movements in various clinical states is due to its action on the spinal cord. Within the spinal cord, the effects appear to be due either to blocking of polysynaptic pathways or to increasing presynaptic inhibition. 11 references. (author abstract modified)

56852
AUTHORS: Arras, Milton J.
ADDRESS: U.S. Naval Hospital, Annapolis, Md.
TITLE: Metabolism of D vs L-dopa.
SOURCE: New England Journal of Medicine.
SOURCEID: 282(14):813, 1970.

In rebuttal to a letter by Sandler, Karoum and Ruthven (New Eng. J. Med., 281:1429, 1969), it is suggested that there is probably an alternate pathway for the metabolism of D-dopa separate from that for L-dopa. In Parkinsonian patients treated with L-dopa, no homogentisic acid was detected in the blood or urine. Using racemic DL-dopa, homogentisic acid was found in both blood and urine. None of the patients studied had alcaptonuria. 4 references.

58235
AUTHORS: Junker, E.
ADDRESS: Universitats-Nervenklinik, 6000 Frankfurt/Main, Niederrad Heinrich Hoffmann-Strasse 10, Germany
TRTITLE: /Exp. psychological study of performance changes with perazine (Taxilan) in mentally disturbed and in healthy experimental subjects following reg. and single dose adm./
TITLE: Experimentell-psychologische Untersuchung von Leistungsveranderungen durch Perazin (Taxilan) bei psychisch gestorten und gesunden Versuchspersonen nach regelmassiger bzw. einmaliger Einnahme.
SOURCE: Nervenarzt (Berlin).
SOURCEID: 41(3):118-123, 1970.

The effects of perazine (Taxilan) upon performance in the 3 areas of thought, perception, and motor performance are reported. The population tested was composed of mentally disturbed patients and a control group of students; the groups were further separated into patients receiving a single dose of 100mg, 3 X 100mg, and 6 X 100mg daily for intervals from 1 to 4 weeks, with the control group receiving 50mg, 100mg, and placebo in a single daily dose. In the thought area, the patients on the drug encountered difficulties in concentration and performed less adequately than the placebo patients; this effect was also observed in the controls. In the field of perception, difficulties began to occur after the second week of treatment in both groups, although the students considered it fatigue. Fine motor coordination and acceleration of motor fatigue were more apparent in the patients than in the control group. 10 references. (author abstract modified)

58240
AUTHORS: Stern, G. M.; Hunter, K. R.; Laurence, D. R.; Armitage, P.
ADDRESS: University College Hospital Medical School, London W.C.1, England
TITLE: Amantadine in parkinsonism.
SOURCE: Lancet (London).
SOURCEID: No. 7657:1127-1129, 1970.

A controlled trial of amantadine hydrochloride 100mg b.d. in 17 patients with parkinsonism showed a small beneficial effect on physical signs but no significant effect on functional disabilities. Improvement in physical signs was maintained for 8 weeks, but several

patients noted deterioration in functional performance after 2-5 weeks of treatment. Amantadine has only slight therapeutic effects compared with L-dopa. 6 references. (author abstract)

58241
AUTHORS: Parkes, J. D.; Zilkha, K. J.; Marsden, Philip; Baxter, R. C. H.; Knill-Jones, R. P.
ADDRESS: Dept. of Neurology, King's College Hospital, London S.E.5, England
TITLE: Amantadine dosage in treatment of Parkinson's disease.
SOURCE: Lancet (London).
SOURCEID: No. 7657:1130-1133, 1970.

Forty three patients with parkinsonism were included in a trial of amantadine. Doses of 100, 300 and 500mg per day were given each patient for 2 weeks in random order. Every patient completed the trial. Results confirmed the benefit seen with amantadine in previous trials and showed considerable individual variation in optimum dose, although the preferred dose was 300mg per day, resulting in a 26%reduction in initial disability score. The results at each dose level were independent of age, sex, duration of disease, concurrent medication or type of disease. The response to amantadine at each dose level was greatest in the most disabled patients. Side effects suggestive of atropine intoxication were seen in a quarter of the patients at some stage of the trial but could be abolished in some cases by reducing or stopping concurrent medication with benzhexol. 10 references. (author abstract modified)

58243
AUTHORS: Barbeau, Andre; Friesen, Henry.
ADDRESS: Clinical Research Institute of Montreal, Montreal, Canada
TITLE: Treatment of Wilson's disease with L-dopa after failure with penicillamine.
SOURCE: Lancet (London).
SOURCEID: No. 7657:1180-1181, 1970.

Because of the beneficial results elicited with L-dopa in treatment of similar nervous disorders, it appeared worthwhile to attempt to treat a patient with hepatolenticular degeneration (Wilson's disease) with L-dopa. When admitted, the patient (17-years-old) had marked rigidity, a constant flapping tremor of all limbs and was unable to enunciate words or care for herself in any way. After 2 months of L-dopa (1000mg/day) plus Ro-4-4602 (200mg/day) she could eat alone, get up from a chair and walk with the aid of callipers. When L-dopa was increased to 1250mg/day, she had difficulty swallowing, became catatonic and had frequent oculogyric crises. Medication was stopped until these symptoms disappeared and then was reinstated at 300mg/day L-dopa and 150mg/day Ro-4-4602. The patient regained the benefits and was discharged. 9 references.

58282
AUTHORS: Cloetens, W. J. H.; Cretallaz, J. C.; Depaepe, A.; Bertholet, G.
ADDRESS: 81 Rue de Neerpede, Brussels 7, Belgium
TRTITLE: /Clinical investigations of the action of a phospholipid complex from cerebral cortex on cerebral circulation disturbances./
TITLE: Klinische Untersuchungen uber die Wirkung eines Phospholipid- komplexes aus Rinderhirn bei zerebralen Durchblutungsstorungen.
SOURCE: Medizinische Welt (Stuttgart).
SOURCEID: 21(12):510-515, 1970.

A cerebrophospholipid complex (lecithin, colamine -cephalin, phosphatidic acid, lecithin and cephalin hydrolyzates, sphingomyelin, triglyceride) used in human therapy is described, together with results of this treatment. Out of 23 elderly patients with

alterations of nervous and psychiatric behavior, 17 showed extremely good improvement. In 9 of these cases, the improvement was due to an amelioration of the nerve cell metabolism and should establish this preparation as an effective means for regeneration of nerve tissue. Since, according to the literature, some traumas slow up CNS phosphatide synthesis, it follows that the slowing up of this synthesis in old age also leads to a state of metabolic and toxic cerebral disturbances (as seen in trauma), and the improvement due to therapy in the 9 patients becomes understandable. The other 8 patients seem to have improved due to improved cerebral circulation or cardiovascular circulation or both. 47 references. (author abstract modified)

58312
AUTHORS: Tricoire, J.; Passeron, J. P.; Lafont, H. .
ADDRESS: Hopital de Bicetre, 78, rue du General-Leclerc, 94 Kremlin-Bicetre, France
TRTITLE: /The employment of a new benzodiazepine, Ro 5-4556 in internal medicine./
TITLE: Emploi d'une nouvelle benzodiazepine, le Ro 5-4556 en medecine interne.
SOURCE: Semaine Therapeutique (Paris).
SOURCEID: 46(1):51-54, 1970.

The mode of action of Ro-5-4556 (a new benzodiazepine), in a study of 300 patients with various diagnoses is described. It was judged to be good in anxiety; very good in agitation, irritability and sleep disturbances; and moderate in the deeper personality disorders, depression or dysthymia - dysphoria. The tolerance was good, and somnolence was manifested at the outset of treatment. The drug was found to be helpful in cases of obesity and was effective in the treatment of mental symptoms accompanying organic disease, particularly in thyroid disease. Depressions of exogenous origin were particularly responsive to this drug. The acute psychological manifestations of alcoholism respond well to this therapy, and the drug does not modify fundamental personality traits. 8 references. (author abstract modified)

58313
AUTHORS: Renault, P.
ADDRESS: Author address not given
TRTITLE: /Dogmatil: a new illumination on the psychological problems of senescence./
TITLE: Le Dogmatil: un eclairage nouveau sur les problemes psychologiques de la senescence.
SOURCE: Semaine Therapeutique (Paris).
SOURCEID: 46(1):87-88, 1970.

A new pharmaceutical preparation, Dogmatil, with antipsychotic properties together with antidepressant effects is described. This drug is well tolerated and has no toxic hepatorenal effects, nor does it affect arterial tension, glycemia or neurovegetative activity. For these reasons, it is particularly applicable in the treatment of senescent ailments. Some of the emotional aberrations accompanying old age, such as self-depreciation, guilt feelings and depressivemoods are particularly responsive to this therapy. It is also recommended for the purpose of breaking the vicious cycle in the thought processes of the aged and focusing their attention on their surroundings with a renewed interest.

52457
AUTHORS: Paillace, Louis A; Snyder, Solomon H.; Weingartner, Herbert.
ADDRESS: Department of Psychiatry, Johns Hopkins University School of Medicine, 725 North Wolfe Street, Baltimore, Maryland 21205
TITLE: 2,5-Dimethoxy-4-methylamphetamine: clinical evaluation of a new hallucinogenic drug.
SOURCE: Journal of Nervous and Mental Disease.
SOURCEID: 150(2):119-126, 1970.

2,5-Dimethoxy-4-methylamphetamine (DOM) was identified by the Food and Drug Administration in samples of STP. Initial reports in the news media indicated that this compound produced prolonged hallucinogenic effects. This study evaluated some of the psychological and physical effects of DOM. Twelve healthy subjects, normal male graduate students, were admitted to the Medical Research Ward of The Johns Hopkins Hospital. In a double-blind design 6 received tap water placebo and 6 received the active compound DOM. Subjects were administered a series of physiological and psychological tests. Anxiety, depression, and obsessive - compulsive and somatic symptoms were measured. In addition, the occurrence of euphoria, dysphoria, and LSD-like symptoms were monitored. The scales used were a symptom questionnaire, consisting of 240 items, and the symptom checklist, consisting of 64 items. There were no marked physiological changes in pulse rate, blood pressure, oral temperature, or pupillary diameter. The symptom checklist indicated that there were significant differences between the placebo group and the drug group. The drug group scored significantly higher on the anxiety, obsessive - compulsive, and somatic scales. The symptom questionnaire also indicated significantly increased scores for the drug group on the LSD-like symptom and euphoria and dysphoria scales. The data from this study indicated that low doses of DOM produced significantly increased feelings of anxiety, euphoria, dysphoria, with somatic and LSD-like symptoms when compared to the control group. The drug did not produce any marked changes in blood pressure, pulse rate, temperature, or pupillary diameter. 14 references. (Author abstract)

54715
AUTHORS: Lloyd, David.
ADDRESS: Hospital for Sick Children, Adolescent Clinic, Toronto, Canada
TITLE: Drug misuse in teenagers.
SOURCE: Applied Therapeutics.
SOURCEID: 12(3)19-25, 1970.

One of the important problems among today's adolescents is the misuse of drugs. At the Hospital for Sick Children in Toronto, there is an increasing need to understand more about the problem. The more commonly used drugs and treatments are discussed below, and suggestions are offered for dealing, in an office practice, with a boy or girl misusing drugs. The emphasis is on several things: (1) there are 3 common drug types in use by teenagers in Toronto: marijuana, LSD25, and the amphetamines; (2) marijuana appears to be relatively harmless and seldom needs treatment; (3) LSD25 is usually found in combination with other drugs and for that reason chloropromazine is specifically warned against, valium is the drug of choice; and (4) recent research has shown amphetamines to be dangerous in their direct effects on body cells. In all cases, personnel treating the drug user should be particularly careful to avoid revealing any hostility toward the patient. It is very important, though often difficult, to show understanding and avoid judging the patient. 7 references.

58448
AUTHORS: Simopoulos, A. M.; Pinto, Alcides; Babikov, Paul W.;

Kurland, A.; Savage, Charles.
ADDRESS: Crownsville State Hospital, Crownsville, Maryland
TITLE: Psychotomimetic properties and therapeutic potentials of dexoxadrol on convalescing alcoholics.
SOURCE: Diseases of the Nervous System.
SOURCEID: 31(3):203-207, 1970.

Dexoxadrol in doses of 75-150mg was given to 18 male alcoholics under a 1 session treatment arrangement to observe the psychotomimetic and psychodelic properties and possible therapeutic effects. The psychodelic-like reaction was brief and not very intense. Shortly after the experiment most patients reported that they were feeling better and more optimistic. After 9 months information obtained from 9 of 18 patients showed 2 of these reporting sobriety. Dexoxadrol appeared to induce catharsis; it may be a more suitable drug for narcoanalysis than barbiturates. 12 references. (author abstract modified)

58454
AUTHORS: Thatcher, Karen; Kappeler, Thomas; Wisecup, Philip; Fischer, Roland.
ADDRESS: Author address not given
TITLE: Personality trait dependent performance under psilocybin (Part II).
SOURCE: Diseases of the Nervous System.
SOURCEID: 31(3):181-192, 1970.

Hallucinations are defined as experiences of intense sensations (S) during which the ability for verification through voluntary motor (M) performance is damped or blocked. After administration of 160microgram/kg psilocybin to 16 college age volunteers, the high sensory to motor (S/M) ratio implicit in a hallucinatory experience was quantified. Handwriting area and handwriting pressure were chosen as sensory and motor parameters for the computation of sensory to motor ratios. The mean handwriting area increased from pre-drug to drug peak while the mean handwriting pressure decreased for 13 volunteers and increased for 3 volunteers. There was a differentiation between the 13 "perceivers", characterized by a high S/M ratio during their psilocybin - induced intensely hallucinatory experiences and the 3 "judgers" who attempt to maintain a low S/M ratio at drug peak and whose response to psilocybin results in a controlled, shorter, non-hallucinatory experience. Another result was the personality trait dependent nature of the dissociation which prevails between the extent of drug - induced autonomic activity and the extent and direction of drug -induced perceptual and behavioral change. The dissociationis not carried by the judgers but is carried almost entirely by the perceivers. 30 references. (author abstract modified)

58914
AUTHORS: Gershon, Samuel.
ADDRESS: Dept. of Psychiatry and Neurology, New York University School of Medicine, New York, N. Y. 10016
TITLE: On the pharmacology of marihuana.
SOURCE: Behavioral Neuropsychiatry.
SOURCEID: 1(10):9-18, 1970.

The available literature on marihuana is examined with specific reference to its chemistry and animal pharmacology in an attempt to provide a comprehensive base for further elucidation of the problems confronting society in this area. A brief botanical description is offered. Some constituents of marihuana resin consist of cannabinol, cannabidiol and tetrahydrocannabinol. The latter is pharmacologically active. A detailed review of marihuana's biological activity is presented. 54 references.

51530
AUTHORS: Dahlberg, Charles C.
ADDRESS: William Alanson White Institute of Psychiatry, New York, N. Y.
TITLE: "Let's stop lying about drugs".
SOURCE: Medical Economics.
SOURCEID: Special Issue:112-117, 140, April 20, 1970.

Half truths and myths concerning drugs are discussed. The psychedelic drugs may sometimes ease depression, though lysergic acid diethylamide (LSD) induces regression which can produce depression. Though amphetamines may ease depression, the depression is only postponed and then intensified when the person is coming down from his high. Some drug users claim that with drugs sex is better. Hallucinogenic drugs only distort perceptions. Large doses of heroin decrease sexual appetite, and small doses may delay ejaculation. Large doses of amphetamines may seriously reduce potency. That LSD and other psychedelic drugs have no clinical use is incorrect. Some psychiatrists feel that LSD can be of considerable value if accompanied by psychotherapy. There is also evidence of value for the use of LSD in treating chronic alcoholism. LSD has been favorably used in the management of terminal cancer patients. The trouble with all of these drugs is that they lead away from life. A drug user may feel love on an LSD trip, but he must return to the reality of the pressures and tensions of everyday life.

51784
AUTHORS: Houser, Norman W.; Richmond, Julius B.
ADDRESS: Inner City Project, San Diego, Calif.
TITLE: Drugs: facts on their use and abuse.
SOURCEID: New York, Lothrop, Lee & Shepard, 1970. 47 p. $3.95.

The use and abuse of drugs is discussed with a view to providing concise, accurate answers to questions about the various stimulants, depressants, hallucinogens, narcotics, and other chemicals on the drug scene and to describe their effects on the body and mind. The problem of drug abuse is viewed in an effort to discourage experimentation with and the use of dangerous substances that might be tempting to youth. Topics considered include chemicals and the body, the difference between drug users and drug abusers, the amphetamines and barbiturates, the hallucinogens (LSD, peyote and mescaline, psilocybin and psilocin, dimethyltryptamine, and STP), the marihuana controversy (description and identification, dependence and other effects of abuse, marihuana compared with tobacco and alcohol, the question of legalizing marihuana, and some medical and legal views), the narcotics, volatile chemicals, the law and drug control, and individual, societal and legal consequences to be considered before deciding to experiment with drugs. 8 references.

56113
AUTHORS: Martin, William R.
ADDRESS: NIMH Addiction Research Center, Lexington, Ky.
TITLE: Pharmacological redundancy as an adaptive mechanism in the central nervous system.
SOURCE: Federation Proceedings.
SOURCEID: 29(1):13-18, 1970.

Evidence is presented that pharmacological redundancy may exist in the central nervous system and that it may be a mechanism in producing certain types of drug tolerance and dependence. The depression of certain functional pathways produced by large doses of neurohumoral antagonists can be surmounted by increasing stimulus strength. The redundancytheory requires that continuing activity of the drug is necessary for the hypertrophy of the redundant pathway and the development of tolerance and physical dependence. Several lines of evidence are presented to indicate that the degree of morphinelike dependence is related to the strength of agonistic

activity and that the pharmacological activity of morphine persists in the tolerant animal. Four pharmacological mechanisms (cholinergic, adrenergic, tryptaminergic, and 5-hydroxytryptophanlike) have been identified which facilitate the flexor factor and evoke the stepping reflex, both being signs of morphine dependence and abstinence. Consequences of pharmacological redundancy that may be important to the issues of tolerance and dependence are discussed. 17 references. (author abstract modified)

58327
AUTHORS: Baumgarten, H. G.; Bushart, W.
ADDRESS: Abtlg. fur Neuroanatomie, Anatomisches Institut der Universitat, Hamburg, Germany
TITLE: Treatment of narcolepsy with mono-amino-oxidase inhibitors and sympathomimetic agents.
SOURCE: European Neurology (Basel).
SOURCEID: 3(2):97-104, 1970.

Experiences gained in three selected forms of narcoleptic syndrome with monoamine oxidase inhibitor (MAOI) therapy, nialamide, in combination with ephedrine, a cerebral stimulant of the amphetamine group, have shown that almost all symptoms can be favorably influenced by activating catecholamine and serotonin metabolism. Electroencephalographic diagrams confirm the therapeutic effect. On the basis of nialamide treatment, waking activity is brought about with far smaller doses of ephedrine, and it remains more stable than under ephedrine alone. Side effects include increased menstrual flow, slight fluor, loss of hair, sweating. 27 references. (author abstract modified)

58397
AUTHORS: Crow, T. J.
ADDRESS: Department of Physiology, University of Aberdeen, Scotland
TITLE: Enhancement by cocaine of intra-cranial self-stimulation in the rat.
SOURCE: Life Sciences.
SOURCEID: 9(7):375-381, 1970.

Bipolar tungsten electrodes were implanted in the ventral midbrain tegmenta of 7 rats which were trained to lever press. The animals were run for 2 hr sessions, after 1 hr of which either cocaine hydrochloride or saline was given intraperitoneally. The cocaine (5mg/kg) produced a clear enhancement of response rate, similar to the stimulatory effect of the amphetamines. The actions of cocaine and the amphetamines with respect to the postulated role of central aminergic neurones in the self-stimulation phenomenon may be (1) a sensitization of an aminergic reward system, or (2) that the central catecholamine neurones are not directly involved in the self-stimulation process but that the behavior is facilitated by direct pharmacological release of transmitter from these neurones. 14 references.

52502
AUTHORS: Meyer, Roger E.; DiMascio, Alberto; Stifler, Lawrence.
ADDRESS: Psychopharmacology Laboratory, 700 Harrison Ave., Boston, Mass. 02118
TITLE: Personality differences in the response to stimulant drugs administered during a sleep-deprived state.
SOURCE: Journal of Nervous and Mental Disease.
SOURCEID: 150(2):91-101, 1970.

Twenty normal males were selected for the study. Criterion for selection was based on personality structure. Subjects were made to remain sleepless for at least 22 hours and then were administered one of a number of antifatigue medications. Hypotheses had been formulated predicting differential responses by the two personality types to the sleeplessness state and to the antifatigue medication. Partial confirmation of the hypotheses was obtained. 20 references. (Author abstract)

55628
AUTHORS: Brill, Henry.
ADDRESS: author address not given
TITLE: Drugs and aggression.
SOURCE: Mental Health Digest.
SOURCEID: 2:11-13, 1970.

Possible uses of aggression suppressing drugs are considered as a method of reducing violent crime or at least dealing with the aggression ridden patient suffering from conduct disorder without psychosis. The separation between the biological sciences (including biological psychiatry) and criminology is deplored. It is contended that this separation is a serious barrier to development in both fields and that psychopharmacology has a large potential as a field of research for methods of control of pathologic aggression.

56925
AUTHORS: Lewis, Evan G.; Dustman, Robert E.; Beck, Edward C.
ADDRESS: Veterans Administration Hospital, Salt Lake City, Utah 84113
TITLE: The effects of alcohol on visual and somato-sensory evoked responses.
SOURCE: Electroencephalography and Clinical Neurophysiology (Amsterdam).
SOURCEID: 28(2):202-205, 1970.

Visual and somatosensory evoked responses were recorded in 9 subjects following administration of a placebo or a dose of alcohol of 0.41 or 1.23g/kg. Ingestion of 3 ounces of alcohol significantly

attenuated the late waves of evoked responses recorded from the central areas but had no effect on evoked responses recorded from the occipital area. In some subjects, a hemispheric asymmetry of amplitude in recordings from central areas disappeared after alcohol ingestion. 16 references. (author abstract modified)

57480
AUTHORS: Ables, Murray F.; Eng, Erling W.; Curtin, Mary E.
ADDRESS: Veterans Administration Hospital, Lexington, Kentucky
TITLE: Group treatment of chronic alcoholism with LSD-25: study II.
SOURCE: Newsletter for Research in Psychology.
SOURCEID: 12(2):17-21, 1970..

A single, oral dose of LSD-25 (50, 100-300 or 450-500 micrograms) was given to 39 male patients with primary or secondary diagnosis of chronic alcoholism and absence of severe psychosis, severe brain damage or physical illness. Thirty six similarly diagnosed patients served as controls. In addition to the alcoholism diagnosis, psychiatric diagnoses included neurotic, psychotic and personality disorders. The LSD - treated subjects showed a greater improvement, or a smaller loss of control, than the control subjects for the following variables measured: number of delirium tremens episodes, most days without drinking, number of days worked, number of arrests and number of irregular discharges. 2 references.

58070
AUTHORS: no author.
ADDRESS: author address not given
TITLE: Synthetic drugs used and abused.
SOURCE: Chemical and Engineering News.
SOURCEID: 48(46):26-27, 29, 1970.

The current situation with respect to misuse of synthetic drugs such as amphetamines and barbiturates is discussed. The 3 patterns of amphetamine abuse are identified, as well as the use of amphetamines in combination with barbiturates. Variations in psychological effects of the amphetamines and barbiturates are described. The pharmacology of the drugs is considered briefly.

58371
AUTHORS: Katz, Joseph; Finestone, Stephen C.; Pappas, Michael T.; Fine, Joseph.
ADDRESS: Department of Anesthesiology, Montefiore Hospital, 3459 Fifth Avenue, Pittsburgh, Pa. 15213
TITLE: A double-blind evaluation of capuride (Pacinox) as a presurgical aid to sleep.
SOURCE: Current Therapeutic Research.
SOURCEID: 12(5):255-260, 1970.

A drug which produces pleasant, sound sleep with minimal side effects for preoperative patients is still to be found. A double-blind study in 296 preoperative patients, both male and female, ranging in age from 21 to 73 years, was performed with capuride (Pacinox), 400mg, a new sleeping medication and an identically appearing placebo. Capuride, a nonbarbituate ureide derivative, produced a statistically significant improvement over placebo in the quality, effect and duration of sleep. The more rapid onset of sleep and fewer number of awakenings during the night of patients on capuride were also statistically significant. Further, capuride appeared to reduce anxiety. Finally, capuride has minimal side effects. 5 references. (author abstract modified)

58561
AUTHORS: Bustamante, J. A.; Jordan, A.; Vila, M.; Gonzalez, A.; Insua, A.
ADDRESS: Institute of Neurophysiology and Psychology, Academy of Sciences of Cuba, Havana, Cuba
TITLE: State dependent learning in humans.
SOURCE: Physiology and Behavior (Oxford).
SOURCEID: 5(7):793-796, 1970.

A slide with 8 geometrical shapes was projected for 3 min to 787 students who were instructed to draw during the following 2 min what they remembered. From the students correctly reproducing 5 to 7 items (average performance), 70 were selected for further experiments. On day 1, all subjects were shown a similar set of geometrical shapes. Retrieval was tested immediately and in 2 or 5 consecutive sessions at 48 hr intervals. Drugs (amphetamine 20mg or amobarbital 200mg) or placebo were administered 30 min before learning or retention testing. Control groups took placebo, amobarbital or amphetamine in all sessions whereas in the experimental groups, these were alternated from session to session. Similar results were obtained both in the 3 and 6 sessions experiments. In all control groups the same monotonic forgetting curves were observed. In the experimental groups, regardless of whether the change was from drug (amphetamine or amobarbital) to placebo or from placebo to drug, retrieval was impaired in the second, fourth and sixth session and improved in the third and fifth session. The same results were observed with either drug. 10 references. (author abstract)

58638
AUTHORS: Back, Kurt W.; Oelfke, Sheila R.; Brehm, Mary L.; Bogdonoff, Morton D.; Nowlin, John B.
ADDRESS: Department of Sociology and Anthropology, Duke University, Durham, North Carolina 22706
TITLE: Physiological and situational factors in psychopharmalogical experiments.
SOURCE: Psychophysiology.
SOURCEID: 6(6):749-760, 1970.

Some psychological and physiological reactions to introduction of chlordiazepoxide hydrochloride to an experimental situation involving a conformity trial were investigated. Groups of 4 subjects were selected with either considerable previous acquaintance (friends) or little acquaintance (strangers). In each group, 2 subjects were given an injection of the drug and 2 an injection of saline. Conformity to false group feedback was measured on a Crutchfield-Gerard apparatus and arousal was measured in terms of the plasma free fatty acid (FFA) level. Self-ratings of mood were obtained using the Nowlis adjective check list. It was found that the experimental manipulations of group composition or drug injection did not yield clear cut results unless the subjects were divided according to initial ratings of anxiety. Subjects initially more anxious, who were administered the drug and who were tested as strangers, showed greater conformity to group pressure and a continuous increase in physiological arousal. These conditions were interpreted as being cumulative sources of strain, under which subjects concentrate on monitoring themselves to the exclusion of attending the surrounding events. 14 references. (Author abstract)

51140
AUTHORS: Henschler, D.; Broser, Fritz; Hopf, H. C.
ADDRESS: Institut fur Toxikologie und Pharmakologie der Universitat, 87 Wurzburg, Koellikerstrasse 2, Germany
TRTITLE: /"Polyneuritis cranialis" following poisoning with chlorinated acetylenes while handling vinylidine copolymers./
TITLE: "Polyneuritis cranialis" durch Vergiftung mit chlorierten Acetylenen beim Umgang mit Vinylidenchlorid-Copolymeren.
SOURCE: Archiv fur Toxikologie (Berlin).
SOURCEID: 26(1):62-75, 1970.

Two workers developed persistent cranial nerve disorders after attempting to clean out tank cars in which an aqueous dispersion of vinylidene chloride copolymers had been transported. Principally involved was the trigeminal nerve; to a lesser degree the occipital auricular and cervical cutaneous nerves as well as the muscles of mastication, the eye muscles and the hypoglossus were affected. The cause of the poisoning was identified to be monochloroacetylene or dichloroacetylene which are present as highly toxic gaseous contaminants in the initial product vinylidene chloride (1,1-dichloroethylene) or developed from contaminants (tetrachloroethane, trichloroethylene) during the production or storage of the product. The mechanisms of formation of these gases are discussed, along with previously reported cases of neuropathy resulting from impure trichloroethylene used as an anesthetic, analgesic or solvent. 38 references. (author abstract)

51373
AUTHORS: Maynard, Robert C.
ADDRESS: Washington Post, Washington, D. C.
TITLE: FDA warns against uses of 'behavior' amphetamines.
SOURCE: Washington Post.
SOURCEID: 93(299):Section A, p. 3, October 15, 1970.

A discussion is presented of the warning of physicians in Omaha, Nebraska, by Federal Food and Drug Administration (FDA) officials against their use of 2 amphetamines to curb the behavior of hyperactive children. The drugs involved were Tofranil (imipramine hydrochloride) and Aventyl (nortriptyline). Neither drug should be used in children and the FDA said that it now specifically warns against such use. Side-effects of Tofranil include constipation, difficulty in focusing the eyes, precipitation of glaucoma, nausea, vomiting, and mild symptoms of parkinsonism, among others. Side-effects of Aventyl include fall in blood pressure, tremors, and bleeding into organs. The FDA indicated that use of these drugs in children would be possible on an experimental basis, but only if a special permit were obtained.

56059
AUTHORS: Rossmann, Heinz.
ADDRESS: Badische Anilin- & Soda-Fabrik AG, 6700 Ludwigshafen am Rhein, Germany
TRTITLE: /A case of probable hematomyelia caused by chronic benzene poisoning./
TITLE: Uber einen Fall wahrscheinlicher Hamatomyelie bei Benzolismus.
SOURCE: Archiv fur toxikologie (Berlin).
SOURCEID: 26(1):56-61, 1970.

A case of chronic benzene poisoning is described in which the resulting neurologic lesion was provisionally regarded to have been syringomyelia. The apparent sudden onset, the lack of progression, the complete absence of signs of dysraphia, and the relatively advanced age of manifestation all point to hematomyelia as the cause of the lesion, which in turn follows as a consequence of the increased bleeding tendency associated with benzene poisoning. The

patient committed suicide 12 years after the onset of the illness. Unfortunately, a post-mortem examination was not carried out. Other reports dealing with further neurological problems connected with proven or suspected benzene poisoning are discussed. 6 references. (author abstract)

56060
AUTHORS: Klavis, G.; Drommer, W.
ADDRESS: Innere Medizin, 3000 Hannover, Bertastrasse 4-6, Germany
TRTITLE: /Goodpasture syndrome and the effects of benzene./
TITLE: Goodpasture-Syndrom und Benzineinwirkung.
SOURCE: Archiv fur Toxikologie (Berlin).
SOURCEID: 26(1):40-55, 1970.

The damage to organs seen in Goodpasture syndrome, which remains difficult to interpret as to its etiology, is similar to that occurring in special cases of heavy exposure to benzene. On the basis of a case study following benzene poisoning, as well as experimental studies on rats using normal and electron microscopic interpretation, it could be shown that poisonings with benzene deserve special attention due to their seriousness and poor prognosis, and that the clinical and pathological findings are similar to those of Goodpasture syndrome. 32 references. (author abstract)

56350
AUTHORS: Harper, M. A.; Earnshaw, B. A.
ADDRESS: University of Queensland Dept. of Psychological Medicine, Clinical Sciences Building, Royal Brisbane Hospital, Queensland 4029
TITLE: Combined adrenal and thyroid deficiency (Schmidt's syndrome) presenting as an acute psychosis.
SOURCE: Medical Journal of Australia (Sydney).
SOURCEID: 1(11):546-548, 1970.

A case history is presented of a woman (40-years-old), with a history of myxedema, who developed Addison's disease and became acutely psychotic. Her disturbed mental state led to her admission to a psychiatric unit. Her psychotic symptoms were initially suggestive of an acute functional psychosis and overshadowed the less prominent clinical features of hypothyroidism. Chlorpromazine, given initially to control vomiting (10mg, 3 times/day) and later for the psychotic symptoms (50mg), probably precipitated the circulatory collapse which was the other main feature of this case. Chlorpromazine, given to patients with hypothyroidism may lead to coma and the patient's report of extreme drowsiness on receiving small doses suggests that she was unusually sensitive to this drug. This case illustrates the difficulties of identifying combined endocrine difficulties and lends support to the observation that phenothiazines are contraindicated in the control of psychoses which may be secondary to thyroid deficiency. 11 references. (author abstract modified)

56611
AUTHORS: Warren, Richard J.; Rimoin, David L.; Sly, William S.
ADDRESS: Division of Medical Genetics, Washington University School of Medicine, St. Louis, Missouri 63110
TITLE: LSD exposure in utero.
SOURCE: Pediatrics.
SOURCEID: 45(3):466-469, 1970.

In spite of the many reports on the damaging effects of LSD on human chromosomes in vitro and in vivo, a report is presented on a clinically normal child with a normal karyotype who was exposed to LSD repeatedly during the first 4 months of fetal life. The mother discontinued LSD ingestion after she found out she was pregnant but continued use of cannabis. Leukocyte cultures were started on both parents and on the 8-month-old infant 5 weeks after the father

ingested 800 micrograms and the mother ingested 320 micrograms of LSD. Lymphocytes from a patient with Franconi's anemia (positive control) and from one of the authors (negative control) were simultaneously cultured. Numerous breaks were found in the chromosomes from the positive control. The chromosomes from both parents, their child, and the negative control lacked abnormal chromosomal associations or a significant number of breaks. The only unusual finding was a large number of micronuclei scattered individually and sometimes in groups in the cells cultured from the father's blood. 14 references.

57978
AUTHORS: no author.
ADDRESS: author address not given
TITLE: Hallucinogens and narcotics alarm public.
SOURCE: Chemical and Engineering News.
SOURCEID: 48(7):44-45, 1970.

Of all the drugs popularly abused today, probably none are viewed with more alarm by the general public than are hallucinogens and narcotic analgesics. Some of the hallucinogens are lysergic acid diethylamide (LSD), mescaline, psilocybin, STP or (DOM) (2,5-dimethoxy-4-methylamphetamine) dimethyltryptamine, and its analog, diethyltryptamine. Like mescaline and psilocybin, LSD is capable of producing profound perceptual alterations. Its action is largely on the central nervous system but as yet no satisfactory mechanism can be agreed on. High doses taken early in pregnancies variably produce deformation in newborn of some animals but not in others. The possibility of chromosome damage in humans has also been explored. The major narcotics are derived from the opium poppy (Papaver somniferum) indigenous to parts of Asia. Narcotic analgesics include naturally occurring opium alkaloids, semisynthetics, and a number of synthetic compounds with morphinelike activity. They include morphine, heroin, codeine, methadone, meperidine, and propoxyphene. The opioids are unsurpassed in their ability to relieve moderate or severe pain. Unfortunately, pharmacologists have been unable to divorce addiction potential from the analgesic properties of these drugs. Life expectancy among opiate addicts is considerably diminished by poor hygiene, adulterated samples, faulty nutrition, and secondary infections. Overdosing is frequent. With chronic use, tolerance develops to the sedative, respiratory, and analgesic effects. On withdrawal, an abstinence syndrome develops which can be eliminated with methadone at doses that do not produce euphoria.

58034
AUTHORS: Adlerfligel; Govaerts, A.
ADDRESS: author address not given
TRTITLE: /Considerations on several side-effects of medicaments (study of 11,410 cases received in the Belgian Center of Anti-poisons)./
TITLE: Considerations sur quelques effets secondaires des medicaments (Etude portant sur 11,410 appels recus au Centre belge anti-poisons).
SOURCE: Bulletin de Medecine Legale et de Toxicologie Medicale (Lyons).
SOURCEID: No. 1:34-41, 1970.

With normal dosage or overdose of medicinal products, substance and dosage are usually presumed or estimated rather than known. In 11410 cases treated in Belgium, 167 registered side-effects which could be reasonably attributed to the drug used, within the limits of the physician's knowledge. Classification of side-effects is made according to the responsible drugs, neuroleptics, analgesics, antibiotics, tranquilizers and hypnotics, antihelminthics, anticholinergics, vitamins, antiepileptics, hormones, and metoclopramide. Unexpected symptoms which seem to result from the usage of medicaments should be recognized for the purpose of distinguishing unpleasant, but not serious, side-effects from

symptoms which cause alarm.

58212
AUTHORS: Appleton, William S.; Shader, Richard I.; DiMascio, Alberto.
ADDRESS: Massachusetts Mental Health Center, 74 Fenwood Road, Boston, Mass.
TITLE: Ocular (pigmentary) effects of psychotropic drugs.
SOURCE: Connecticut Medicine.
SOURCEID: 34(1):25-28, 1970.

The complications of psychotropic drugs which are associated with pigmentation are reviewed. Chlorpromazine has been noted to cause eye and skin pigmentation, with involvement of the lens and cornea in particular. Incidence varies depending on dosage, climate, patient sample and pathological criteria. Pigmentation occurs in the following sequences: anterior lens, posterior cornea, anterior cornea, conjunctiva and the retina. Epithelial keratopathy was observed in 20 of 30 schizophrenic patients taking 2000mg/day chlorpromazine. This condition differs from the previously mentioned condition in that is is related to high daily dosages rather than to total dosages. Only 6 of these patients showed corneal and lenticular changes. Pigmentary retinopathy has been produced secondarily by chlorpromazine, but it is principally associated with large doses (1200mg/day) of thioridazine. In a study of 27 patients on high doses of phenothiazine, 5 were found to have lesions of the fundus, and 5 had lesions confined to the cornea and lens. Pigmentation of the cornea and lens are irreversible or at best only partially reversible. This condition does not interfere with visual acuity except in the more advanced cases. 27 references.

58213
AUTHORS: Sachs, Frederick L.; Landsberg, Lewis; Brooten, Pamela.
ADDRESS: Yale University School of Medicine, New Haven, Conn.
TITLE: A case of manic-depressive illness with lithium toxicity.
SOURCE: Connecticut Medicine.
SOURCEID: 34(1):36-39, 1970.

A discussion is presented of the case of a 54-year-old woman who was hospitalized for diabetic ketoacidosis. She had been taking lithium carbonate (300mg 5 times daily). Lithium blood levels on admission were between 0.54 and 0.72meq/l. The patient convalesced well until the twenty ninth hospital day, when she was noted to be markedly obtunded with hyperflexia, tremulousness, myoclonic jerks and unsustained ankle clonus. Serum lithium levels were elevated to 3.04meq/l. Cerebral spinal lithium level was 1.24meq/l. Lithium was discontinued, and the patient began a saline diuresis. On the thirty third day, her serum lithium level was 0.49meq/l. The lithium toxicity went unnoticed, since daily readings of the serum level were not taken. Factors implicated included a water deprivation test given during her hospital stay, severe diarrhea and a large diuresis. The physiological effects and the uses of lithium are discussed. 5 references.

58333
AUTHORS: Royds, R. B.; Knight, A. H.
ADDRESS: Luton and Dunstable Hospital, Luton, Bedfordshire, England
TITLE: Tricyclic antidepressant poisoning.
SOURCE: The Practitioner (London).
SOURCEID: 204(1220):282-286, 1970.

Three cases of tricyclic antidepressant poisoning, in which each patient developed hyperglycemia, are reported. Peritoneal dialysis was found to be useful; full serum, urine and dialysate levels of the ingested drug were estimated. Complications in 1 case included ingestion at the same time of monoamine oxidase inhibitors and alcohol, and in another, of barbiturates. Experience with these cases indicates that such patients should be continuously monitored

for cardiac arrhythmias, half - hourly urine testing for glycosuria is useful, while forced diuresis and peritoneal dialysis are both effective forms of treatment. 2 references.

58365
AUTHORS: Rozman, Robert S.; Kurland, Arnold A.
ADDRESS: Department of Pharmacology, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, D. C. 20012
TITLE: The effect of flurothyl and electroshock on pulmonary diffusion.
SOURCE: Behavioral Neuropsychiatry.
SOURCEID: 2(1,2):20-22, 1970.

Flurothyl (bis(2,2,2-trifluoroethyl)ether) is one of the newer convulsants being used therapeutically. Since it is routinely administered by inhalation, it was deemed advisable to determine its effects on pulmonary function. Pulmonary diffusion using fractional uptake and diffusing capacity of carbon monoxide was determined in 27 controls and 62 schizophrenic patients. The patients received either electroconvulsive therapy, flurothyl by inhalation, flurothyl by intravenous injection, or some combination of these. No consistent effect on pulmonary diffusion was seen with any treatment. The individual personal reactions of a patient seemed to be the major cause of change in experimental results. 2 references.
(authorabstract modified)

58403
AUTHORS: Sacks, O. W.; Messeloff, C.; Schartz, W.; Goldfarb, A.; Kohl, M.
ADDRESS: Beth Abraham Hospital, Bronx, New York
TITLE: Effects of L-dopa in patients with dementia.
SOURCE: Lancet (London).
SOURCEID: No. 7658:1231, 1970.

In a letter to the editor a report is made of 3 Parkinsonian patients with impaired cognitive function (dementia) who, after receiving less than 4g L-dopa daily for two months, presented massive dissociation and disintegration of cortical function. This syndrome was one of agitated hallucinatory delirium, accompanied by severe chorea and motor unrest. It is suggested that these reactions to L-dopa may be subdivided into 3 components: a primary subcortical excitation induced by the drug; a cortical "driving" enforced by this; and finally, a massive breakdown of functional integrity in the cortex. Within a month of withdrawal of L-dopa all had returned to their original neurological and mental status. It is hoped that suboptimal doses of L-dopa (less than 2g daily) may reduce parkinsonian disability somewhat, without producing overexcitement.

58405
AUTHORS: Fries, Hans.
ADDRESS: Department of Psychiatry, Academic Hospital, Uppsala, Sweden
TITLE: Lithium in pregnancy.
SOURCE: Lancet (London).
SOURCEID: No. 7658:1233, 1970.

The use of lithium in pregnancy has been questioned and the experimental findings on the possible teratogenicity of lithium are contradictory. A case is presented of a 26-year-old woman who had recurrent endogenous depression since 1963, had made several suicide attempts, and had become stabilized on lithium treatment since 1967. In 1970 she gave birth to a normal, well developed child with lithium treatment being continued during and after pregnancy. Just prior to delivery the serum lithium of the mother was 0.9 meq/liter and the concentration in umbilical blood was the same. One week after delivery the lithium level in her milk was 0.3 meq/liter, and the level in the child's serum was likewise. It appears lithium crosses

the placental barrier completely in man. Other brief remarks are made of possible teratogenicity of lithium and of the necessity to register births where lithium salts are used. 4 references.

58422
AUTHORS: Edgley, Robert.
ADDRESS: 25 Falcon St., Crows Nest, N. S. W. 2065, Australia
TITLE: Diazepam, nitrazepam and the N. H. S.
SOURCE: Medical Journal of Australia (Sydney).
SOURCEID: 1(4):186-187, 1970.

Diazepam and chlordiazepoxide cause habituation and addiction problems, a fact not generally known to all physicians and pharmacists. Withdrawal symptoms such as tremor, agitation and hypomanic reaction have been seen. Similar problems have occurred with glutethimide, amphetamines, barbiturates, bromides, chloral hydrate and nitrazepam. Therefore, a good deal of consideration must be given before diazepam's National Health Service restrictions are modified. However, thioridazine should have its specified purposes modified, since this drug could remove many addiction problems.

58442
AUTHORS: Hansbrough, E. T.
ADDRESS: Kneibert Clinic, Poplar Bluff, Missouri 63901
TITLE: Hallucinations following pentazocine.
SOURCE: Missouri Medicine: Journal of the Missouri State Medical Association.
SOURCEID: 67(8):602, 608, 1970.

Pentazocine (Talwin), approved for use by the FDA in 1967, has value as a postoperative pain control. Addiction (after i.m. injection) and epileptiform abnormality (after i.v. administration of 3 to 5 times the analgesic dose) have recently been reported. Hallucinogenic properties have been estimated to be manifest in less than 1 in 1000 cases. Four case reports (26 to 77 year old patients) of hallucination (3 after 30mg i.m. and 1 after 50mg p.o. administration) are described: the three incidents with i.m. injection occurred after the first dose, while oral administration of the drug was hallucinogenic after the second dose (the first having induced sleep). All cases of hallucination were frightening visual experiences. In spite of these side-effects, pentazocine has filled a real need in postoperative pain control. 6 references.

58451
AUTHORS: Hanlon, Thomas E.; Ota, Kay Y.; Kurland, Albert A.
ADDRESS: Maryland Psychiatric Research Center, Baltimore, Maryland 21228
TITLE: Comparative effects of fluphenazine, fluphenazine-chlordiazepoxide and fluphenazine-imipramine.
SOURCE: Diseases of the Nervous System.
SOURCEID: 31(3):171-177, 1970.

A comparison was made of the effectiveness of fluphenazine-placebo, fluphenazine-chlordiazepoxide, and fluphenazine-imipramine in the treatment of 211 newly admitted psychiatric hospital patients. Along with placebo, chlordiazepoxide, imipramine and fluphenazine were administered in a double-blind manner, 40mg, 100mg and 6.6mg daily, respectively. Measures of treatment effects included standard psychiatric interview and ward behavior scales, global estimates of degree of illness and improvement, physical symptom ratings, and total and subtest scores on a brief form of the Wechsler Adult Intelligence Scale. The characteristic effect of chlordiazepoxide was to attenuate the antipsychotic action of the phenothiazine employed as the base drug. Imipramine had a slight beneficial effect in patients initially displaying symptoms of depression. The addition of imipramine to fluphenazine was not associated with an increase in frequency or severity of side reactions. 12 references. (author abstract modified)

58455
AUTHORS: Witztum, Joseph; Baker, Max; Woodruff, Robert A., Jr.; Pitts, Ferris N., Jr.
ADDRESS: Department of Psychiatry, Washington University School of Medicine, Saint Louis, Missouri
TITLE: Electrotherapy: the effects of methohexital on EKG.
SOURCE: Diseases of the Nervous System.
SOURCEID: 31(3):193-195, 1970.

Four doses methohexital (0.6, 0.7, 0.8, 0.9mg/kg) used to induce electroconvulsive therapy (ECT) anesthesia were studied using electrocardiograms (EKG). In 48 patients, ages 21-69 years, post - electroconvulsive therapy EKG abnormalities were probably not a consequence of the dose of methohexitol in the range studied. There were no significant differences in the duration of any procedure periods with any doses of methohexital except for briefer seizures with highest dose compared to the lowest dose. A starting dose of 0.75 mg/kg is reasonable for methohexital in ECT anesthetic induction. There is no evidence that this dose produces prolonged post-convulsive apnea or an increased incidence of EKG abnormalities in comparison with other methohexital doses studied. 3 references.

58527
AUTHORS: Inniss, Charles N.
ADDRESS: Poison and Adverse Drug Reaction Team, University Hospital, Ann Arbor, Michigan
TITLE: U-M team issues warning on use of drug.
SOURCE: Michigan State Medical Society Journal.
SOURCEID: 69(15):692-693, 1970.

The University of Michigan Medical Center is attempting to delete Glutethimide (Doriden) from their formulary and is urging Michigan physicians to cease prescribing the drug as a routine sedative. Glutethimide has been implicated in fatalities, from both accidental and intentional overdoses. Victims are difficult to treat; the lack of dialyzability of Glutethimide and its lipophilic nature prolong its toxic effect. The efficacy of Glutethimide as a sedative is not sufficiently greater than other less potentially lethal sedatives.

58534
AUTHORS: Weintraub, Michael I.; Gaasterland, Douglas; Van Woert, Melvin H.
ADDRESS: Department of Neurology, Yale-New Haven Medical Center, New Haven, Connecticut 06510
TITLE: Pupillary effects of Levodopa therapy.
SOURCE: New England Journal of Medicine.
SOURCEID: 5(5):120-123, 1970.

A patient with Parkinson's disease and subclinical postganglionic Horner's syndrome developed anisocoria during chronic oral L-dopa therapy. The mechanism of action of L-dopa and dopamine on the sympathetic innervation of the eye was investigated. Five patients, one of whom had a postganglionic Horner's syndrome without Parkinson's disease, served as controls. Topical dopamine and chronic systemic L-dopa produced pupil dilatation only in eyes with intact sympathetic innervation. Single large doses of L-dopa had no effect on the pupil size. L-dopa and topical dopamine appear to produce pupillary dilatation indirectly, through a peripheral increase in activity of intact sympathetic pathways, and not through direct alpha receptor stimulation. 14 references. (author abstract modified)

58589
AUTHORS: Rothstein, Emil; Clancy, David D.
ADDRESS: Brockton Veterans Administration Hospital, Brockton, Massachusetts
TITLE: Combined use of disulfiram and metronidazole in treatment of alcoholism.
SOURCE: Quarterly Journal of Studies on Alcohol.
SOURCEID: 31(2):446-447, 1970.

In a double-blind study, disulfiram (500mg daily for a month, then 250mg daily) was given to 58 hospitalized male alcoholics for an average of 3 months; metronidazole (750mg daily, 250mg daily after psychoses developed in 6) was also given to half the group, and placebo to the other half. Drinking episodes, staff assessment of patients, and self-reports of patients were evaluated. Essentially identical results were observed in both groups; metronidazole in no way aided in the treatment. Six of the 29 patients who received metronidazole developed an acute confusional psychosis which was reversible but contraindicated the combined use of the drugs. 8 references. (author abstract)

58908
AUTHORS: Lucas, George J.; Lehrnbecher, Wolfgang.
ADDRESS: Neurogenetics Section, Overholser Div. of Clinical Research, Public Health Service, DHEW, Washington, D. C.
TITLE: Chromosomal effects of LSD-25, a controversy?
SOURCE: Journal of the Arkansas Medical Society.
SOURCEID: 66(10):348-349, 1970.

Cytogenetic findings seem to support results of recent articles that show no increase of chromosome breakages caused by LSD. Using a modification of the method described by Moorhead and coworkers (1960), lymphocytes from patients were cultivated and then treated with Colcemid. There was a suppression of mitosis recognized in three cases. Additional radioautographic studies failed to show any change of a normal labeling pattern of replication in the experimental cultures as compared to controls. Minor chromosomal damage might remain undetected with present techniques. 15 references.

58951
AUTHORS: Yost, Murray A., Jr.; McKegney, F. Patrick.
ADDRESS: Yale-New Haven Hospital, New Haven, Connecticut
TITLE: Acute organic psychosis due to Talwin (pentazocine).
SOURCE: Connecticut Medicine.
SOURCEID: 34(4):259-260, 1970.

A 25-year-old male, a known narcotic addict using cocaine daily for several years, was admitted to the hospital with a diagnosis of acute Candida albicans endocarditis with aortic valve involvement. His medications included 60mg daily i.v. Amphotericin, 0.25mg daily digoxin, and Talwin, 50mg i.v. every 4 hrs for chest pain. Severe chest pain developed after aortic valve replacement, for which he received high doses of Talwin. On the sixth postoperative day, he became increasingly tremulous and slightly confused. He was given Elavil (25mg t.i.d.) for sleeplessness and depression. By the twelfth postoperative day, he began experiencing occasional auditory and visual illusory and hallucinatory phenomena and was placed on Trilafon (4mg) and Cogentin (0.5mg q.i.d.). At this time, the patient was receiving 230mg of Talwin daily. On the fourteenth day, Talwin was discontinued on the basis of a possible diagnosis of acute toxic psychosis, possibly drug related. On the fifteenth day, the Elavil, Trilafon and Cogentin were withheld. By the eighteenth and nineteenth days, the symptoms were completely resolved. It is suggested that in this case, high doses of Talwin over a long period of time were responsible for the serious complication of acute toxic psychosis. 6 references.

57473
AUTHORS: Fujimoto, James M.; Wang, Richard I. H.
ADDRESS: Department of Pharmacology, Marquette School of Medicine, Milwaukee, Wisconsin 53233
TITLE: A method of identifying narcotic analgesics in human urine after therapeutic doses.
SOURCE: Toxicology and Applied Pharmacology.
SOURCEID: 16(1):186-193, 1970.

Alkaloids were separated from urine in 15 min with an Amberlite XAD-2 resin column, and the methanol eluate was chromatographed on 2 thin layer silica gel glass microfiber sheets to establish a pattern of spots for each narcotic analgesic and its metabolites. A detailed description of the method is given. One hundred forty coded urine samples were collected from 6 controls and 134 others receiving narcotic analgesics. Six control samples were correctly demonstrated to contain no alkaloids. The remaining 134 samples were positive to iodoplatinate and of these 134, 88 were identified correctly to be 27 meperidine, 29 codeine, 2 morphine, 1 levorphanol, 27 pentazocine, and 2 dihydromorphinone samples. In the remainder, 13 could not be assigned to a specific narcotic analgesic, and 33 were misidentified. These errors are discussed. 7 references. (author abstract modified)

58364
AUTHORS: Kellner, Robert.
ADDRESS: Department of Psychiatry, University of New Mexico, School of Medicine, Albuquerque, New Mexico
TITLE: The design of drug trials with neurotic patients.
SOURCE: Behavioral Neuropsychiatry.
SOURCEID: 2(1,2):12-19, 1970.

The literature of drug trials with neurotic patients was surveyed and designs of these trials were tabulated and related to outcome. Since several variables other than design determine the results of a drug trial, and various features of the design are interdependent, no definite conclusions can be drawn about the extent to which any one variable affected the outcome. There may be a time period in a drug trial in which differences between the effects of two treatments are most marked; the differences may not be apparent at an earlier or later stage of the trial. 121 references. (author abstract modified)

51117
AUTHORS: Schreiber, Eric C.
ADDRESS: Drug Metabolism Dept., Squibb Institute for Medical Research, New Brunswick, N. J.
TITLE: The metabolic alteration of drugs.
SOURCE: In: Elliott, H., Annual review of pharmacology.
SOURCEID: Palo Alto, Calif., Annual Reviews, 1970. 505 p. Vol. 10. (p. 77-98).

A review is presented of studies on the metabolic alteration of drugs. The role of drug metabolism in the investigation of substances of therapeutic interest has undergone considerable change in the past decade. Drug metabolism can be of immense value and will contribute substantially toward a meaningful interpretation, as well as a scientifically acceptable explanation, of biologic responses observed by pharmacologists, pathologists, and toxicologists. Improperly applied, it is too easy to assume that the biological half-life measured in the rat is also that which will be seen in the human, or that the liver of a dog will produce the same metabolites (and in the same amounts) as the liver of a woman. The papers reviewed for this study cover mescaline, diethylpropion, pronethalol, perazine, norepinephrine and epinephrine metabolites, and the in vivo and in vitro metabolism of diazepam and chlordiazepoxide. 77 references. (author abstract modified)

51118
AUTHORS: Hucker, Howard B.
ADDRESS: Merck Institute for Therapeutic Research, West Point, Pa.
TITLE: Species differences in drug metabolism.
SOURCE: In: Elliott, H., Annual review of pharmacology.
SOURCEID: Palo Alto, Calif., Annual Reviews, 1970. 505 p. Vol. 10. (p. 99-118).

A review is presented of the literature on species differences in drug metabolism. It is not yet possible to predict, in other than a few instances, the metabolic fate of drugs in various species. Most studies in the field of drug metabolism have been descriptive in nature, and almost no work on the detailed mechanism involved has been reported. Recent discovery was made of the essential role of liver microsomes and cofactors in drug metabolism. Other aspects awaiting further exploration are comparative metabolism studies in the higher primates and interspecies comparison of drug metabolite levels at the site of action. 196 references. (author abstract modified)

51120
AUTHORS: Goz, Barry; Prusoff, William H.
ADDRESS: Dept. of Pharmacology, Yale University School of Medicine, New Haven, Conn.
TITLE: Pharmacology of viruses.
SOURCE: In: Elliott, H., Annual review of pharmacology.
SOURCEID: Palo Alto, Calif., Annual Reviews, 1970. 505 p. Vol. 10. (p. 143-170).

A review is presented of the literature on the pharmacology of viruses. Only 2 new antiviral agents have been approved by the FDA for therapy in man, idoxuridine (IUDR, IDU, 5-iodo-2'-deoxyuridine) and amantadine (adamantanamine.HCl, Symmetrel). Examples of 2 contrasting methods for design of drugs that have been successful are the synthesis of effective antimalarials and of British anti-lewisite (BAL). Through the combined efforts of British and American organic chemists, thousands of potential antimalarials were synthesized, a fact that resulted successfully in the finding of efficacious compounds. In contrast, BAL represented 1 of the 1st few compounds synthesized in an attempt to find an effective antidote to the lethal poison agent lewisite. BAL was designed on a rational basis because appropriate effort went into elucidation of the biochemical mechanism

for the toxicity of lewisite. Adequate molecular understanding resulted in appropriate or relevant synthesis. Similar biochemical understanding of the malarial parasite was not and is still not available. A strong effort is being made today to attain understanding of animal virus formation and composition at the molecular level as well as an understanding of the biochemistry of the host virus interrelationship. 240 references. (author abstract modified)

51121
AUTHORS: Weiner, Murray; Piliero, Sam J.
ADDRESS: Geigy Pharmaceuticals, Division of Geigy Chemical Corporation, Ardsley, N. Y.
TITLE: Nonsteroid anti-inflammatory agents.
SOURCE: In: Elliott, H., Annual review of pharmacology.
SOURCEID: Palo Alto, Calif., Annual Reviews, 1970. 505 p. Vol. 10. (p. 171-198).

A review is presented of the literature on nonsteroid antiinflammatory agents. The events of the inflammatory process, experimental approaches to the study of inflammation, antiinflammatory agents, and a report of new agents are included. There has been no dramatic breakthrough in our understanding of inflammation or in antiinflammatory drugs in recent years. Steady increases in experience, particularly in relation to immune phenomena, and the correlation of subcellular ultrastructure and biochemistry give promise of major advances in the understanding and treatment of inflammatory disease in the near future. 284 references. (author abstract modified)

51122
AUTHORS: Temple, T. Eugene; Liddle, Grant W.
ADDRESS: Dept. of Medicine, Vanderbilt University, Nashville, Tenn.
TITLE: Inhibitors of adrenal steroid biosynthesis.
SOURCE: In: Elliott, H., Annual review of pharmacology.
SOURCEID: Palo Alto, Calif., Annual Reviews, 1970. 505 p. Vol. 10. (p. 199-218).

A review is presented of the literature on inhibitors of adrenal steroid biosynthesis. There have been numerous developments in adrenocortical pharmacology during the past 2 decades, yet much remains to be learned about the intimate biochemical mechanisms through which various agents inhibit the biosynthesis of corticosteroids. In the process of elucidating these mechanisms it may be possible to gain some insight into the basic nature of the inborn errors of metabolism which at least superficially resemble the pharmacologic inhibition of adrenal function. As long as there are people who might benefit by reduction of their levels of mineralocorticoids, glucocorticoids, androgens, or estrogens, there will be at least a theoretical need for safe, effective, selective inhibitors of steroid biosynthesis. 122 references. (author abstract modified)

51123
AUTHORS: Diassi, Patrick A.; Horovitz, Zola P.
ADDRESS: The Squibb Institute for Medical Research, New Brunswick, N. J.
TITLE: Endocrine hormones.
SOURCE: In: Elliott, H., Annual review of pharmacology.
SOURCEID: Palo Alto, Calif., Annual Reviews, 1970. 505 p. Vol. 10. (p. 219-236).

A review is presented of the literature on endocrine hormones. Rather than discuss the more popular areas of endocrine pharmacology, such as the adrenal and gonadal hormones, insulin, and the catecholamines, a decision was made to limit this review to some of the less popular and newer hormones. Topics covered include pineal hormone, thyroid hormones, hypothalamic hormones, gastrointestinal

hormones, insect hormones, plant hormones, and the prostaglandins. 162 references. (author abstract modified)

51125
AUTHORS: Mirkin, Bernard L.
ADDRESS: Depts. of Pharmacology and Pediatrics, Clinical Pharmacology Section, University of Minnesota, Minneapolis, Minn.
TITLE: Developmental pharmacology.
SOURCE: In: Elliott, H., Annual review of pharmacology.
SOURCEID: Palo Alto, Calif., Annual Reviews, 1970. 505 p. Vol. 10. (p. 255-272).

A review is presented of the literature on developmental pharmacology. Ontogenesis in the mammalian cell reflects a continuum of integrated biochemical events initiated by fertilization, sustained by implantation and placentation, and susceptible to environmental influences. Numerous investigations in this area have created a massive, primarily descriptive literature, tending to emphasize correlations between the morphologic rather than biochemical effects of teratogenic and embryopathic drugs. It seems desirable that the actions of pharmacologic agents on developing biologic systems be viewed from a perspective which permits not only the analysis of drug effects upon embryogenesis but also allows for an evaluation of how physiologic maturation basically influences the disposition of and response to pharmacologically active molecules. 99 references. (author abstract modified)

51126
AUTHORS: Weiner, Norman.
ADDRESS: University of Colorado Medical Center, Denver, Colo.
TITLE: Regulation of norepinephrine biosynthesis.
SOURCE: In: Elliott, H., Annual review of pharmacology.
SOURCEID: Palo Alto, Calif., Annual Reviews, 1970. 505 p. Vol. 10. (p. 273-290).

A review is presented of studies on the complex effects which various physiological and pharmacological inputs may have on the metabolism of the adrenergic neurotransmitter, norepinephrine. Although the rate and regulation of norepinephrine synthesis is emphasized, other aspects of the metabolism of norepinephrine (storage, release, catabolism) are also analyzed with the realization that analogous complex interactions are virtually inevitable. An appreciation of this may be acquired either in general reviews of this subject, or in reviews which focus on special features of adrenergic nervous system physiology, such as false transmitters, uptake processes, release mechanisms, and the storage of catecholamines. 170 references. (author abstract modified)

51128
AUTHORS: Himwich, Harold E.; Alpers, Hilma S.
ADDRESS: Thudichum Psychiatric Research Laboratory, Galesburg State Research Hospital, Galesburg, Ill.
TITLE: Psychopharmacology.
SOURCE: In: Elliott, H., Annual review of pharmacology.
SOURCEID: Palo Alto, Calif., Annual Reviews, 1970. 505 p. Vol. 10. (p. 313-334).

A review is presented of the literature on psychopharmacology. In treatment of schizophrenia, a careful study revealed that the differences between psychotherapy plus drugs and drugs alone are often very small or trivial and are never statistically significant. The clinical effectiveness of the antianxiety drugs is somewhat controversial because of a number of confounding variables which are nondrug in origin. There seems to be a consensus that in the management of anxiety, meprobamate, chlordiazepoxide, diazepam, and oxazepam are slightly better than barbiturates, and all are somewhat better than placebo. Various members of the imipramine group of

drugs have shown superiority over placebo in the treatment of depressed patients. With further information on the biochemical aspects of psychotic or endogenous depression, more specifically directed therapy and improved clinical results may be expected. 202 references. (author abstract modified)

51133
AUTHORS: Lasagna, Louis.
ADDRESS: Division of Clinical Pharmacology, Johns Hopkins Hospital, Baltimore, Md.
TITLE: Challenges in drug evaluation in man.
SOURCE: In: Elliott, H., Annual review of pharmacology.
SOURCEID: Palo Alto, Calif., Annual Reviews, 1970. 505 p. Vol. 10. (p. 413-420).

A discussion is presented of challenges in drug evaluation in man. After centuries of clinical evaluation of drugs that proceeded primarily by trial-and-error and serendipity, the field of clinical pharmacology has begun to develop, during the last 2 decades, principles and techniques that will ultimately provide a scientific basis to drug development and use. A brief description is given of some important areas of drug evaluation that deserve special attention and emphasis. 16 references. (author abstract modified)

51572
AUTHORS: Roth, Martin; Schapira, Kurt.
ADDRESS: Dept. of Psychological Medicine, Univ. of Newcastle upon Tyne, England
TITLE: Social implications of recent advances in psychopharmacology.
SOURCE: British Medical Bulletin (London).
SOURCEID: 26(3):197-202, 1970.

Pharmacological therapies, developed during the last 20 years, have had clear and important social implications. The effectiveness of phenothiazine compounds in the control of acute schizophrenia has contributed to shortened hospitalization. There is evidence, further, that phenothiazines administered to chronic schizophrenics, play a part in the normalization of their social behavior. The introduction of monoamine oxidase inhibitors and tricyclic compounds promised relief for the depressions and a possible reduction in suicide rates. There has been rapid progress during the last decade in humanizing mental hospitals. Psychiatric units within general hospitals are treating patients with acute mental disorders. Open hospitals, whose staff is increasingly involved in aftercare, the provision of day hospitals, and industrial rehabilitation units are becoming increasingly characteristic of the psychiatric scene in Britain. A general movement has developed toward the creation of a more homelike, small scale kind of residential care. Unlike drugs such as heroin and amphetamines, the drugs recently introduced for the control of anxiety show little tendency to give rise to a dependency syndrome. Through experience in the treatment of mental disorders and emotional distress, many doctors have learned the limitations as well as the benefits of drug treatment. 34 references.

51593
AUTHORS: Dollery, C. T.; Davies, D. S.
ADDRESS: Dept. of Clinical Pharmacology, Royal Postgraduate Medical School, London, England
TITLE: The conduct of initial drug studies in man.
SOURCE: British Medical Bulletin (London).
SOURCEID: 26(3):233-236, 1970.

The decision to proceed to clinical trial of a new therapeutic agent must be justified on several grounds. Most often, animal studies suggest a potential application to therapy. Toxicity evidence must show that dangers in the drug have been assessed. The dose and route of administration should be carefully considered.

Increasingly, early studies are carried out by trained clinical pharmacologists in laboratories which are staffed to meet any emergency. The amount of information that can be obtained can be much improved by the use of good experimental design, including the use of controls. It is best to avoid combined drug treatment in the early stages of a new drug investigation. When sufficient experience has been accumulated with the new drug alone, it is then desirable to conduct investigations of drug interactions likely to occur in practice. Steps should be taken to monitor the volunteers and patients who take the drug. It has become common practice to carry out blood counts, serum electrolytes, and urea determination, and tests of liver function before and after new drugs are administered. If a serious reaction occurs which may be due to the drug, it is essential to investigate the patient and the circumstances as thoroughly as possible. 10 references.

52517
AUTHORS: Howard, Kay; Nickels, Karl; Mock, John E.; Lipman, Ronald S.; Covi, Lino; Bauman, N. C.
ADDRESS: Dept. of Psychiatry, Philadelphia General Hospital, Phila., Pa.
TITLE: Therapeutic style and attrition rate from psychiatric drug treatment.
SOURCE: Journal of Nervous and Mental Disease.
SOURCEID: 150(2):102-110, 1970.

This study attempted to identify and explore those therapist attributes which might be related to low socioeconomic class patients dropping out of psychiatric drug treatment, a widely recognized problem. Six experienced psychiatrists were observed during their initial treatment sessions with approximately 225 neurotic outpatients participating in a double blind, placebo controlled psychiatric drug evaluation study. Patients were primarily of low socioeconomic class, female, and Negro. The observers rated items related to therapists' behavioral activity, characteristics, reactions, general style, and therapeutic activity on either 4 or 7 point scales. The data were approached in two ways. One set of analyses compared three therapists with relatively low dropout rates with three therapists with relatively high dropout rates, using only patients who completed the study. In a second set of analyses, patients were divided into two groups, completers and dropouts; therapists were pooled; and styles of treatment with these two patient groups were compared. All therapists were rated as somewhat more active and involved in therapeutic activity and as having a warmer relationship with completers than with dropouts. It was suggested that the therapists' approach to treatment might fruitfully be described in terms of a bipolar continuum, ranging from activity to passivity. It was further suggested that more active involvement of therapists and greater attempts to involve patients actively in the treatment process seem to decrease dropout rates even in situations where drugs are considered to be the central treatment agent and the population consists of low socioeconomic class patients. 12 references. (Author abstract)

55325 $03
AUTHORS: Long, J. P.; Chiou, C. Y.
ADDRESS: Dept. of Pharmacology, College of Medicine, Univ. of Iowa, Iowa City, Iowa 52240
TITLE: Pharmacological testing methods for drugs acting on the peripheral nervous system.
SOURCE: Journal of Pharmaceutical Sciences.
SOURCEID: 59(2):133-148, 1970.

Pharmacological testing methods for drugs acting on the peripheral nervous system are reviewed. Bioassay techniques are described in some detail, since the same biological preparations are often used to study the sites of drug effects on the peripheral nervous system. The principal biological preparations used for this

purpose are discussed. The synaptic vesicle and synaptosomes are presented as newly developed preparations with high potential for solving the mechanism of drug actions at nerve terminals. 139 references.

56575
AUTHORS: Wurtman, Richard J.
ADDRESS: Author address not given
TITLE: Catecholamines and neurologic diseases.
SOURCE: New England Journal of Medicine.
SOURCEID: 282(1):45-46, 1970.

The reported effects of catecholamines on neurologic disorders are reviewed. Many patients with Parkinsonism show striking and sustained improvement when treated with L-dopa. Brain dopamine levels are depressed in untreated patients with Parkinsonism. Chronic manganese poisoning symptoms also improve after L-dopa treatment. Apomorphine also has rapid ameliorating effects in patients with Parkinsonism, which suggests that whole families of new drugs for treatment of this disorder await discovery. Little is known about the fate of administered L-dopa in animal or in man. It is decarboxylated to dopamine somewhere in the body. Much of the compound is O-methylated before it is converted to dopamine and is therefore wasted. The lack of evidence of excessive sympathetic tone is compatible with the observations that less than 1% of administered L-dopa is converted to norepinephrine. The neurotransmitters of neurons other than the catecholaminertic neurons await identification. Once these compounds are known, it is possible that their levels will also be found to vary with specific neurologic diseases. 7 references.

56748
AUTHORS: Scardino, Joseph.
ADDRESS: Saint Vincent's Hospital, 144 West 12th Street, New York, N. Y.
TITLE: Lithium in affective disorders.
SOURCE: New York State Journal of Medicine.
SOURCEID: 70(5):638-642, 1970.

Lithium was first tested as an antipsychotic drug in 1949. Its biphasic action (therapeutic in the manic phase and prophylactic in the depressive phase), makes it the first truly specific psychiatric drug. The changes lithium causes in the electrolyte balance may result in functional changes in the central nervous system. The main clinical application is for affective disorders, but it has also been used for epilepsy, excitement states, premenstrual syndrome and induced psychoses. Its greatest effectiveness is as an antimanic agent. Advantages of lithium treatment include rapid control, effectiveness in chronic resistant cases, prevention of recurring manic and depressive episodes, no addiction or withdrawal, inexpensiveness and low toxicity. Disadvantages include remissible electrocardiographic changes, proteinuria, hematuria and degenerative renal changes. 21 references.

56750
AUTHORS: No author.
ADDRESS: Author address not given
TITLE: Elusive epileptic pattern traced.
SOURCE: Medical World News.
SOURCEID: 11(1):30E, 1970.

Absence status, or absence continuing, is a form of generalized epilepsy often misinterpreted by laymen and overlooked by physicians. It is described by Dr. Frederick Andermann as seen by him and Dr. J. Preston Robb, both of the Montreal Neurological Institute. On the basis of long-term histories and EEG findings, these physicians have been able to distinguish absence status from conditions easily confused with it such as epileptic prodromes, postictal confusion,

toxic states, hysterical behavior and others. Also, absence status usually appears with other seizure patterns such as generalized or myoclonic seizures or absence attacks. Absence status is described and differentiated from absence attacks. Treatment of absence status is less of a problem than is diagnosis. Intravenous diazepam or barbiturates are most effective in terminating or shortening the attacks.

56997
AUTHORS: No author.
ADDRESS: Author address not given
TITLE: Do alkaloids hook alcoholics?
SOURCE: Medical World News.
SOURCEID: 11(8):23, 1970.

Although the law still considers that alcoholism is as much a paralysis of will power as anything else, research on alcoholism has perhaps too long emphasized the psychological aspect. It is time for more intensive study of the role of alcohol in development and maintenance of this disease process in the susceptible drinker. The physiological basis for alcoholism to be an addictive disease is the direct action of acetaldehyde, the initial metabolite of alcohol, on enzymes that metabolize catecholamines, the neurotransmitters. One recent hypothesis suggests that acetaldehyde and noradrenaline may interact directly to produce a psychoactive morphine-like alkaloid of the tetrahydroisoquinoline family. A new theory now suggests that alcohol may indirectly interfere with brain biochemistry to produce another tetrahydroisoquinoline alkaloid. It is suggested that alcoholics are not so much addicted to alcohol, but to self-induced addictive substances.

57012
AUTHORS: No author.
ADDRESS: Author address not given
TITLE: Of spots and psychosis.
SOURCE: Medical World News.
SOURCEID: 11(11):4-5, 1970.

The appearance of blue, mauve and red "spots" in the urine of LSD users and psychotic patients during chromatographic analysis has been identified as kryptopyrrole. Kryptopyrrole does not occur in nature, has not been traced to any specific source and is not associated with diet, tobacco or phenothiazines. It is believed to be important in the possible diagnosis of psychosis and in understanding the basic mechanism of the psychotic disease process.

57029
AUTHORS: Goldberg, Leonard.
ADDRESS: Department of Alcohol Research, Karolinska Institute, Stockholm, Sweden
TITLE: Effects of ethanol in the central nervous system.
SOURCE: In: Popham, R.; Alcohol and alcoholism.
SOURCEID: Toronto, University of Toronto Press, 1970. 421 p. (p. 42-56).

This paper is devoted to a discussion of subjective and objective effects of ethanol on the central nervous system based on experiments in voluntary subjects. Special reference is given to subjective mood ratings and objective performance, including standing, steadiness and certain ocular phenomena (positional alcohol nystagmus; roving ocular movements). Topics discussed include interaction between alcohol and drugs; postalcoholic effects ("hangover"); and the relation between effects and blood alcohol. 15 references.

57030
AUTHORS: Murphree, H. B.; Price, L. M.

ADDRESS: Department of Psychiatry, Rutgers Medical School, New Brunswick, New Jersey
TITLE: Electroencephalographic effects of some alcoholic beverages.
SOURCE: In: Popham R., Alcohol and alcoholism.
SOURCEID: Toronto, University of Toronto Press, 1970. 421 p. (p. 57-62).

The subjects included 4 men and 5 women, ages 22 to 36, who were occasional to moderate drinkers by American standards. Electroencephalographic recordings were made for 10 minutes before dosage, for 30 minutes after dosage, then for 10 minutes of each half hour up to 3 hours after dosage. Blood ethanol concentrations were determined, and eye movements were monitored. The beverages taken orally consisted of 80 proof vodka and an 86 proof bourbon. The third alcoholic beverage used was made by fortifying the same kind of vodka with pure congeners prepared gas chromatographically from the same kind of bourbon. The dosages for vodka and bourbon were 1 ml/kg. For the "superbourbon", the dose was 0.25ml/kg. The results indicate that either the congeners themselves have direct, long lasting effects upon the central nervous system as reflected in the EEG, or they may somehow retard the metabolism of ethanol so that it has a stronger and more enduring depressant effect. The latter would seem less probable. One would therefore have to postulate that somehow tissue concentrations were maintained even though blood concentrations were not. Accordingly, it appears more likely that one or more of the congeners have direct depressant effects and that these can be separated from those of ethanol, because the former are much longer lasting. 4 references.

57031
AUTHORS: Fried, Rainer.
ADDRESS: Department of Biochemistry, Creighton University Medical School, Omaha, Nebraska
TITLE: Biochemical studies of a new anti-alcoholic drug, metronidazole.
SOURCE: In: Popham, R., Alcohol and alcoholism.
SOURCEID: Toronto, University of Toronto Press, 1970. 421 p. (p. 63-72).

The new antialcoholic drug metronidazole was studied in vitro with several mammalian enzymes related to alcohol metabolism. The drug inhibited alcohol dehydrogenase and cream and liver xanthine oxidase, as well as uricase. The first 2 enzymes are inhibited only when tetrazolium salts are not included in the reaction mixture. The mechanism of this reaction is not known. Metronidazole causes a much less severe reaction than disulfiram, probably because metronidazole prevents the formation of acetaldehyde, which accumulates when disulfiram is used as an antialcoholic agent. The new drug, which shows promise as an effective antialcoholic agent, has proved to be a valuable tool for the study of alcohol metabolism and for enzyme research. 18 references. (author abstract modified)

57046
AUTHORS: Lundquist, Gunnar A. R.
ADDRESS: Alcohol Research Clinic, Stockholm, Sweden
TITLE: The use of drugs in the treatment of alcoholism.
SOURCE: In: Popham, R., Alcohol and alcoholism.
SOURCEID: Toronto, University of Toronto Press, 1970. 421 p. (p. 170-172).

The medical treatment during the acute stages constitutes treatment of a syndrome, but the medical and psychological treatment after the acute stage is the treatment of a person. The important factor in this stage is the choice of drugs, in order to avoid dependence. Among the drugs most often used for the rehabilitation of alcoholics are chlorprothixene, levomepromazine, thioridazine, fluphenazine and promethazine. In rare cases, it can be very helpful to give the patient amphetamines, dexamphetamines or methylphenidate

for a short time. A second group of drugs that can be used are the sensitizing drugs which make it difficult to drink. Metronidazole has been reported to decrease the craving for alcohol.

57060
AUTHORS: Wieser, Stefan.
ADDRESS: Municipal Clinic for Nervous Diseases, Bremen, West Germany
TITLE: Treatment of the chronic neuropsychiatric complications of alcoholism.
SOURCE: In: Popham, R., Alcohol and alcoholism.
SOURCEID: Toronto, University of Toronto Press, 1970. 421 p. (p. 278-280).

A review of the clinical classification of neuropsychiatric complications of alcoholism is presented. So-called "alcoholic epilepsy" is the link between the psychoses and the neurological complications of chronic alcoholism. The generally accepted treatment schedule for epileptic seizures in chronic encephalopathies in alcoholics is based on the distinction between grand mal and psychomotor seizures. Grand mal seizures are controlled by a combination of hydantoins and barbiturates. Psychomotor seizures are treated with a combination of antiepileptic drugs with an increased amount of barbiturate. Seizures are manifestations of irreversible anatomico-pathological processes.

57242
AUTHORS: Kane, Francis J., Jr.
ADDRESS: Dept. of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, N.C. 27514
TITLE: Current use of hypnotic drugs --is it rational?
SOURCE: Southern Medical Journal.
SOURCEID: 63(4):376-380, 1970.

Recent studies have shown that use of hypnotic agents for relief of sleeplessness continues to be a widespread practice, at least in the United States and England. Recent research in psychopharmacology and the physiology of sleep and dreaming indicates that other drugs, such as minor tranquilizers and antidepressants might be more suitably used. Such therapy would be more specific treatment for the syndrome of which the insomnia is a part, and it would be less likely to produce rebound phenomena and drug dependence. 20 references. (author abstract)

58069
AUTHORS: no author.
ADDRESS: author address not given
TITLE: Legal restrictions hamper drug research.
SOURCE: Chemical and Engineering News.
SOURCEID: 48(48):38-39, 1970.

The problems of the researcher in the area of drug research are considered. Among these are the inability under the law to protect names of informants; extensive paperwork connected with legal authorization by the Internal Revenue Service; obtaining drugs such as marihuana from the National Institute of Mental Health; and political problems as with district attorneys trying to make a name by busting students. The signing into law of the Comprehensive Drug Abuse Prevention and Control Act of 1970 will ease some of these situations but does not become effective until May 1, 1971. Title I provides for broader rehabilitation, treatment, and educational activities by the Department of Health, Education and Welfare; it also protects scientific researchers in drugs from prosecution. Title II is the Controlled Substances Act, giving the Department of Justice authority to control drug abuse on a wide front. Title II also creates a Presidential Commission on Marihuana and Drug Abuse to explore the reasons for drug abuse. Title III provides for control of export and import of drugs and replaces most previous legislation to control illicit drug use.

58145
AUTHORS: Bureau of Narcotics and Dangerous Drugs, Division of Drug Sciences, Office of Science and Drug Abuse Prevention; Broecker, L.; Richards, L.
ADDRESS: U. S. Dept. of Justice, Washington, D. C.
TITLE: Bibliography of research on cannabis (marihuana).
SOURCEID: Washington, D. C., Bureau of Narc. and Dangerous Drugs, 1970. 14 p.

A bibliography of research on cannabis (marihuana) is presented. This bibliography lists studies published in English on the use and effects of the various preparations of the cannabis plant and synthetic tetrahydrocannabinol. All known reports of original research on humans are included, but none of the numerous summaries of research and discussions of the subject are referred to. Those more general expositions are cited in the Bureau of Narcotics and Dangerous Drugs Fact Sheet No. 14 and in other bibliographies. This list is intended for those who need to refer to original sources of findings on cannabis. Many of these reports are available from the Bureau of Narcotics and Dangerous Drugs library. Others are on file in the Division of Drug Sciences and can be borrowed on request. 138 references.

58238
AUTHORS: Voller, Gert W.; Kerstan, Jurgen.
ADDRESS: Konigin Elena-Klinik Neurolog. Klinik und Rehabilitationszentrum fur Parkinsonkranke, 3500 Kassel, Germany
TRTITLE: /The treatment of the Parkinson syndrome with L-dopa./
TITLE: Die Behandlung des Parkinson-Syndroms mit L-Dopa.
SOURCE: Nervenarzt (Berlin).
SOURCEID: 41(3):138-144, 1970.

The Parkinson syndrome is one of the most frequently encountered neurological diseases and its most important manifestations are the extrapyramidal motor disturbances. Through the remarkable progress in the biochemical and histochemical investigations neuropsychiatry also profited in that the metabolic disturbances in the extrapyramidal disorders were investigated. Dopamine was the catecholamine that was most involved in this disorder. The most recent research in this connection has found that the dopamine deficit in the extrapyramidal centers is due to an insufficient synthesis and storage in the ganglionic cells, apparently due to a block in the enzyme. Cotzias attempted to cure this deficit with the introduction of L-dopa (the precursor of dopamine). However, with the high dosage, numerous undesirable side effects occurred. Results with L-dopa therapy (the L-isomer) are presented. 44 references.

58299
AUTHORS: Bienert, H.
ADDRESS: 7057 Winnenden, Schlossstrasse 35, Germany
TRTITLE: /Considerations on the question of home treatment of mental patients with psychopharmaceuticals./
TITLE: Uberlegungen zur Frage einer heimlichen Heilbehandlung psychisch Kranker mit Psychopharmaka.
SOURCE: Medizinische Welt (Stuttgart).
SOURCEID: 21(17):796-804, 1970.

Treatment of mental patients by means of psychopharmaceutical medication in their own homes is discussed. The use of Haloperidol (used in the treatment of some schizophrenias), which is tasteless and odorless and can be mixed with food or drink, was found to have produced severe extrapyramidal dyskinesia in a young man who took it in his beer. The law states that it is the physician's responsibility to advise the patient of any danger connected with the ingestion of a drug, and that this applies to typical dangers only and not to an atypical case. It is pointed out that when the

depressed patient is told about his illness (which may be incurable) and, in addition, is warned about the medication, he is unlikely to go through with the therapy. The subject of how to deal with such therapy is discussed. 21 references.

58308
AUTHORS: Pletscher, A.; Bartholini, G.; Gey, K. F.; Jenni, A.
ADDRESS: F. Hoffmann-La Roche and Co. AG, Forschungsabteilung, Grenzacherstrasse 124, CH-4000, Basel, Switzerland
TRTITLE: /The biochemical principles for the treatment of parkinsonism with L-dopa./
TITLE: Die biochemischen Grundlagen fur die Behandlung des Parkinson- Syndroms mit L-Dopa.
SOURCE: Schweizerische Medizinische Wochenschrift (Basel).
SOURCEID: 100(19):797-804, 1970.

Various findings indicate that dopamine, which occurs in high concentrations in the extrapyramidal brain centers, functions as a neurohumoral transmitter. In Parkinson's disease, a decreased content of dopamine and other biogenic amines has been found in these centers. L-Dopa, the biological precursor of the catecholamines, partially penetrates from the blood into the brain, where it is decarboxylated into dopamine. The amine seems to accumulate preferentially in the extrapyramidal brain centers. The biological lesion in Parkinson's disease can therefore be partially counteracted by L-dopa. The side effects of L-dopa are probably in part due to the fact that biologically active catecholamines (dopamine, noradrenaline and possibly adrenaline) are not only formed in the extrapyramidal brain centers, but also in other brain regions as well as in extracerebral tissues. The chronic toxicity of L-dopa seems to be low. 64 references. (author abstract)

58309
AUTHORS: Kaeser, H. E.; Perel, D.; Wurmser, P.
ADDRESS: Neurologische Universitatsklinik, Socinstrasse 55, CH-4000 Basel, Switzerland
TRTITLE: /Treatment of parkinsonism with L-dopa./
TITLE: Behandlung des Parkinson-Syndroms mit L-Dopa.
SOURCE: Schweizerische Medizinische Wochenschrift (Basel).
SOURCEID: 100(19):805-813, 1970.

With L-dopa, it is possible to influence the specific biochemical defect in parkinsonism, i.e., the reduction of dopamine in the corpus striatum. Since L-dopa, the precursor of dopamine, is for the most part degraded in the periphery, high oral doses (3-6g daily) are required in order to achieve optimal results. All the parkinsonism symptoms, particularly akinesia, can be favorably influenced. According to present experience, a highly purified form of L-dopa, as opposed to the racemate, may be considered atoxic. Side effects are, however, frequent and necessitate gradual adaptation to the dosage. In the initial stage of treatment, gastrointestinal disturbances and orthostatic hypotension are predominant. In long-term treatment, hyperkinesia is the most important dose -limiting factor. Interaction with other therapeutic agents is considered. 48 references. (author abstract modified)

58603
AUTHORS: Il'yuchenok, R. Yu.
ADDRESS: Laboratoriya Neyrofiziologii i Farmakologii Povedeniya Instituta Fiziologii Sibirskogo Otdeleniya AN SSSR, Novosibirsk, Siberia, U.S.S.R.
TRTITLE: /Action of pharmacological agents on memory and learning./
TITLE: Deystvie farmakologicheskikh veshchestv na pamyat' i obucheniye.
SOURCE: Farmakologiya i Toksikologiya (Moskva).
SOURCEID: 33(2):237-246, 1970.

Drugs acting on the mechanism of memory and effects of drugs on

transfer of information from short term memory to long term memory is reviewed. The formation of memory and the resultant processes as structural changes in the neurological synapses, leading to improvement of transmission of impulses in different structures of the brain is explained. The effects of drugs on the proper mechanism of memory results from the blockade of cholinergic mechanisms of the central nervous system and impairment of new traces in synapses. The potentiation of indirectly induced reflexes is not effected after anticholinergic drugs. Blockade in the central nervous system can depress or block the registration and storage mechanisms of memory. However, the presence of conditional reflexes during the blockade of cholinergic receptors with anticholinergic drugs does not support this theory. The most important factor in the processes of memory and training is the competition between anticholinergic substances and acetylcholine released on cholinergic terminals during the response. When the competition for cholinergic receptors favors acetylcholine, the response is present. After repeated exposure of experimental animals to electrical stimuli, the cholinergic receptor can be unblocked by release of endogenous acetylcholine. Anticholinergic drugs block cholinergic receptors in the subsynaptic membrane. A direct relationship between conditional reflexes and the degree of blockade of acetylcholinesterase in the brain was demonstrated. The effect of agonists on training is dependent on change in the synthesis of RNA and metabolism of the brain. The retrograde amnesia after narcosis results from a blockade of ascendent reticular formation; amnesia of this type can be blocked by the stimulation of reticular formation after training. Substances or drugs which affect the cholinergic structures influence the proper mechanism of memory, and produce changes in regulation and formation of memory. 82 references.

58793
AUTHORS: Rowan, A. James; Scott, Donald.
ADDRESS: Electroencephalography Dept., London Hospital, London, England
TITLE: The management of children with epilepsy.
SOURCE: Practitioner (London).
SOURCEID: 204(1219):136-148, 1970.

In the diagnosis of epilepsy in children, a detailed and accurate history and a complete physical and neurological examination are of prime importance. The initial laboratory workup should include a complete blood count, serum calcium, fasting blood sugar, urinalysis, skull X-rays and an EEG. Anticonvulsants should be given gradually, increasing the dosage until the earliest signs of toxicity appear. If fits continue, another drug should be added in gradually increasing amounts along with the first drug. Withdrawal from the drug should also be gradual, since sudden withdrawal may precipitate status epilepticus, which usually occurs in combination with fever, infection or head trauma. Febrile convulsions should be treated promptly with aspirin, cold sponging and phenobarbitone in appropriate dosage, which should be continued if there are more than 2 or 3 seizures. The treatment of infantile spasms and status epilepticus is also mentioned. A therapeutically oriented classification table and a table of the anticonvulsant drugs with appropriate dosages is also presented together with advice for parents of the epileptic child. Management of epilepsy in childhood should be based on careful initial evaluation, conscientious supervision and a resort to appropriate social services. 27 references.

58861
AUTHORS: Murphy, George E.
ADDRESS: Dept. of Psychiatry, Washington University School of Medicine, St. Louis, Mo.
TITLE: Finding the cause of 'imaginary' pain.
SOURCE: Hospital Physician.
SOURCEID: 6(2):107-112, 1970.

If a patient's complaint of pain cannot be explained as a normal one that will disappear in good time, it is likely to have one or more of 3 sources: hysteria, depression and a type of social isolation that is seen alone or in combination with one of the other 2 conditions. Hysteria applies to the condition of women with a multitude of complaints who give a complicated and dramatic clinical history. It is suggested that this type of patient be referred to a psychiatrist for definitive diagnosis and treatment. Depression can be easily recognized by characteristic disturbances in mental, physiological and social functioning. The patient will only complain of one or two of the many symptoms bothering him. Severe depression responds to electroconvulsive therapy; milder forms of depression can be treated with antidepressant medication or monoamine oxidase inhibitors, both of which bring prompt relief from pain. The social isolation syndrome can be treated by institution of proper nursing procedures that will be reassuring and will reestablish the confidence of the patient.

58886
AUTHORS: Pfizer Laboratories.
ADDRESS: Author address not given
TITLE: Doxepin HCl capsules (Sinequan).
SOURCE: Clinical Pharmacology and Therapeutics.
SOURCEID: 11(3):452-454, 1970.

On a carefully designed series of controlled studies, Sinequan (doxepin hydrochloride), a new dibenzoxepin psychotherapeutic agent, has been shown to have marked antianxiety and antidepressant activity. Sinequan is recommended for psychoneurotic patients, alcoholic patients with anxiety and/or depression and patients exhibiting psychotic depressive disorders. Warning, precautions and adverse reactions are discussed. An initial dose of 25mg t.e.d. is recommended for most patients with illness of mild to moderate severity. Potent spasmolytic activity contributes to the pharmacological profile of Sinequan. Sinequan is well absorbed and rapidly metabolized after oral administration. The results of animal toxicology studies are presented.